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Excessive Pricing in the Pharmaceutical Industry: The Leadiant and Aspen cases

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Alla mia famiglia e ai miei amici che

mi hanno sostenuta in ogni passo

verso questo traguardo, vi voglio bene.

A mio papà che mi ha resa la donna che sono oggi,

Ti amo infinitamente. Con te, Per te, Sempre.

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1. Introduction: The Pharmaceutical Industry

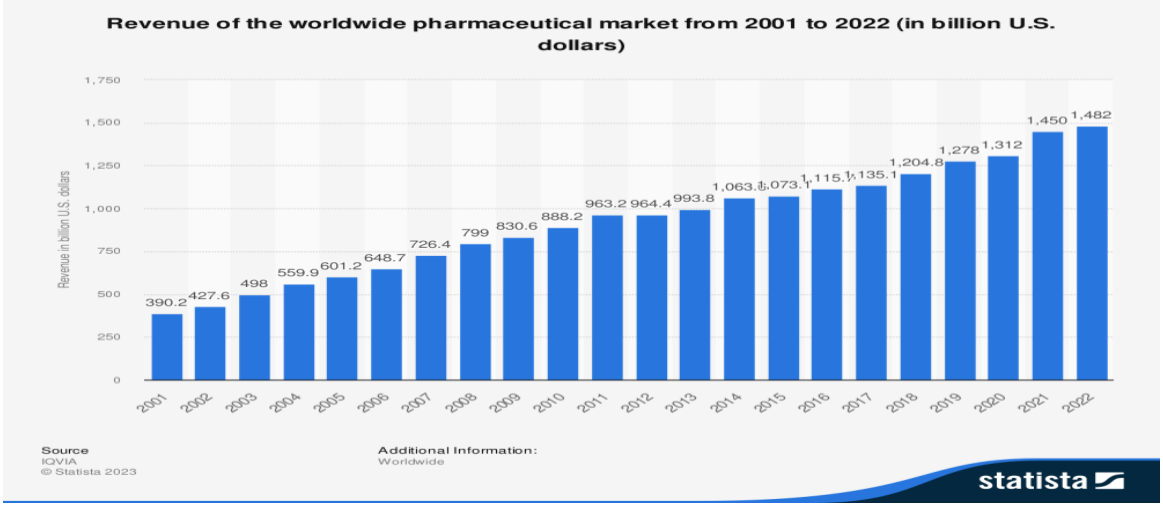
Through the supply of life-saving drugs, treatments, and medical equipment to millions of people, the pharmaceutical industry contributes significantly to the development of the global economy. This industry has a long history, dating back to the early 19th century when scientists began experimenting with natural substances to develop new medicines. Since then, the industry has evolved and grown to become one of the most lucrative and complex sectors in the world. The pharmaceutical sector is made up of businesses that are involved in the research, development, production, and marketing of pharmaceuticals, vaccines, and other healthcare goods. These companies may be involved in every stage of the drug development process, from discovery and preclinical research to clinical trials and regulatory approval. The spectrum of activities includes research and development (R&D) for new active ingredients and dosage forms, the manufacture of pharmaceuticals, and the placing on the market under the company's own name. Competitive dynamics in the industry also derive from the presence of generic medications and medical devices. In fact, pharmaceutical manufacturers can be divided into two groups: original manufacturers and generic manufacturers. The former - also called research-based manufacturers - are characterized by pharmaceutical research and development of new drugs and usually specialize in selected therapeutic areas in which they are market leaders. Generic manufacturers, on the other hand, usually do not do any research, but use active ingredients for which patent protection has already expired and can thus offer drugs at significantly lower prices.

Various laws and regulations govern the process of patenting, testing, and marketing drugs to ensure their safety and efficacy. The industry is highly regulated and is subject to strict quality control standards, safety protocols, and ethical considerations. One of the primary goals of the pharmaceutical industry is to improve the health and well-being of people worldwide. The industry has made significant contributions to healthcare, developing new treatments and cures for a range of diseases and medical conditions. Another key aspect of the pharmaceutical industry is its economic impact. The industry is one of the largest and most profitable sectors in the world, generating billions of dollars in revenue each year (Figure 1). As previously cited, pharmaceutical companies invest heavily in research and development, which can be costly and time-consuming. In fact, as the pharmaceutical industry's product funnel suggests, out of 5,000 compounds in the discovery and preclinical phase, which lasts from three to six years, only 125 leads, and of those just two drugs are tested in the clinical phase, that lasts seven years, to then have only one drug selected for approval. However, successful drugs can generate significant profits, making the industry a high-risk, high-reward business. The industry is characterized by significant barriers to entry, including high costs of research and development, complex regulatory requirements, and long timelines for drug development and

approval. Despite these challenges, the pharmaceutical industry has seen significant growth in recent years, driven in part by the increasing demand for innovative therapies to address unmet medical needs. In 2020, the global pharmaceuticals market generated $1,228.45 billion in revenue from treatments and exhibited a compound annual growth rate (CAGR) of 1.8%. The industry has also seen significant consolidation, with mergers and acquisitions becoming more common as companies seek to expand their portfolios and diversify their revenue streams. The structure of the pharmaceutical industry is also changing as new technologies and business models emerge. For example, the rise of precision medicine and personalized healthcare is driving a shift towards smaller, more targeted drug development programs. Meanwhile, the increasing use of digital health technologies and telemedicine is creating new opportunities for pharmaceutical companies to engage with patients and healthcare providers.

In conclusion, the pharmaceutical industry is a dynamic and complex sector that plays a critical role in global health and the economy. The industry is characterized by a variety of players, including pharmaceutical companies, contract research organizations, academic institutions, regulatory bodies, and healthcare providers. Despite significant challenges, the pharmaceutical industry will continue to grow and innovate as new technologies and business models emerge. At the same time, there is growing public concern over the high cost of prescription drugs, access to healthcare, and the ethics of drug development and marketing which needs to be addressed; being the pharmaceutical industry a vital part of the global economy and playing a critical role in improving human health. Rising drug prices can limit access to care and put significant financial strain on patients and healthcare systems. Excessive pricing in the pharmaceutical industry is both unethical and illegal. We are going to discuss this issue in detail in the next chapters.

Figure 1 Revenues of the worldwide pharmaceutical market from 2001 to 2022 (statista.com)



2. Excessive Pricing in the Pharmaceutical Industry and Antitrust Authorities

2.1 Excessive pricing in the industry

The pharmaceutical industry generates huge profits, and it has experienced remarkable growth in the past two decades, totaling worldwide revenues of 1.48 trillion U.S. dollars in 2022 (see Figure 1). The costs and pricing structure of the market are often opaque; leading to valid concerns regarding the level of innovation and value provided by increasingly costly new treatments. Recent years have seen significant calls for intervention against high prices for pharmaceutical products; policymakers and other stakeholders in many countries have become increasingly concerned about the prices of many drugs. In England, for example, the government is fighting Vertex, a drug company, over the cost of Orkambi, a drug for cystic fibrosis. Also in America, due to the high cost of insulin, which increased by more than 200% between 2007 and 2018[1], a lot of diabetics have died[2]. Despite complaints from poorer countries for decades, it took high-profile dramas in wealthy nations to bring the problem of medicine unaffordability to the forefront of the global health agenda. The abuse of dominant position in the pharmaceutical industry by charging excessive prices, especially for generic medicines, has become a very big issue, to the point that it was the hottest topic at the World Health Assembly (WHA) of 2019. That year Giulia Grillo, the Italian Health Minister, backed by many rich and poor countries, called for action to improve the transparency of prices and R&D costs, as well as the costs of production of medicines, and asked firms to disclose all the different forms of government support they receive; hoping that greater clarity would lower drug prices. She said that the resolution would end "deplorable asymmetries of access to information about many aspects of the innovation and supply chain for medicines, vaccines, and other health technologies"[3]. The stronger commitments around transparency of costs weakened over time, but it is expected that the resolution will continue to help open future discussions on the costs of R&D and clinical trials.

[1] Hirsch, I.B. (2022). Insulin Pricing in the USA: the Saga Continues. *The Lancet Diabetes & Endocrinology*, 10(10). doi:https://doi.org/10.1016/s2213-8587(22)00251-0.

[2] The Economist, (2019). *The global battle over high drug prices*. [online] Available at: https://www.economist.com/business/2019/05/21/the-global-battle-over-high-drug-prices?utm_medium=cpc.adword.pd&utm_source=google&ppccampaignID=18151738051&ppcadID=&utm_campaign=a.22brand_pmax&utm_content=conversion.direct-response.anonymous&gclid=Cj0KCQiA0oagBhDHARIsAI-BbgcSUOUXEbD-xQkpGLr61rx0N7Q0MMD2gMYP67cieqk1timeqwoKz0AaAtemEALw_wcB&gclsrc=aw.ds

[3] Anon, (2019). *WHA Resolution For Transparent Drug Pricing: Italy Speaks Out - Health Policy Watch*. [online] Available at: https://healthpolicy-watch.news/wha-resolution-for-transparent-drug-pricing-italy-speaks-out/.

According to a report by the World Health Organization (WHO), in late 2018, regarding cancer medications, drug companies primarily set prices based on their anticipated revenue rather than on production costs or patient accessibility. The WHO also discovered that despite the high costs associated with drug development, cancer medications yield profits that far exceed R&D costs and the necessary expenses to finance and create incentives for future efforts. Additionally, cancer drugs are more costly than other medicines, presumably because buyers are willing to pay more for treatments of fatal diseases. Australian data reveals that the expense per prescription for cancer medications is at least 2.5 times greater than for other drugs. While it is unsurprising that a business seeks to maximize profits, pharmaceutical companies are not typical enterprises, as their products are essential to saving lives, and they gain exclusive rights to their drugs through government patents, which are granted by society.

2.2 Regulation in the Industry

Pharmaceutical regulations, or medicines regulations, have been defined as "*the combination of legal, administrative, and technical measures that governments take to ensure the safety, efficacy, and quality of medicines, as well as the relevance and accuracy of product information"*[4]. This is fulfilled through a variety of regulatory activities over the course of a drug's life cycle including premarket screening and new pharmaceuticals evaluation, manufacturing facilities inspection, regulation of drug labeling and promotional activities, and the post-marketing surveillance of drugs after approval. The pharmaceutical industry is heavily regulated by policies at both the European Union and national levels. The primary objective is to make sure that people can access affordable and innovative medicines, while also maintaining a competitive environment within the industry. Regulation plays a vital role in defining the characteristics of this industry, particularly in terms of drug pricing and reimbursement schemes, but also of quality and safety. Regulations are required both for new innovations and already existing products, in order to improve health status. In the area of pharmaceutical policies, Member States hold the primary responsibility for determining the conditions under which drugs are purchased by their national health systems (NHS), insurance companies, and patients. National arrangements must carefully balance principles of financial sustainability with the need for new medicines and broader health treatment options. Different policy tools are used by national health systems to establish pricing and reimbursement procedures for

[4] www.sciencedirect.com. (n.d.). *Pharmaceuticals Regulation - an overview | ScienceDirect Topics*. [online] Available at: https://www.sciencedirect.com/topics/pharmacology-toxicology-and-pharmaceutical-science/pharmaceuticals-regulation#:~:text=Pharmaceutical%20regulations%20across%20the%20world.

pharmaceutical products, such as external reference pricing, where a comparison of prices charged in other Member States is made, to derive a benchmark, and the value-based pricing, determined through health technology assessments. While some EU Member States directly control the price of reimbursed medicines, others allow pharmaceutical companies to set initial price levels, with price control exercised indirectly to ensure reimbursement up to a certain amount or under an acceptable price. The EU has enacted secondary legislation to partially harmonize pharmaceutical pricing regulations across its Member States. Directive 89/105/EEC (the "Transparency Directive") establishes specific requirements for transparency, objectivity, and verifiability in pricing and reimbursement procedures. The Directive mandates that pricing and reimbursement decisions comply with a specific timeframe, provide a statement of reasons, and be subject to judicial review. However, the effectiveness of this legislation has been limited, and the European Commission's proposal for amendments in 2012 was ultimately withdrawn due to the absence of a foreseeable agreement with Member States.

In Italy, the Agenzia Italiana del Farmaco (AIFA) is responsible for the regulation of Italian medicines and medical devices by ensuring that they are safe, effective, and of high quality. It was established in 2003 and operates under the supervision of the Italian Ministry of Health, among many roles, it assures innovation, efficiency, and simplification of registration procedures, to guarantee rapid access to medicines[5] and manages the National Pharmaceutical Formulary (PFN). AIFA also monitors the safety of medicines already on the market and takes action if any safety concerns arise. In addition to its regulatory functions, it is also responsible for managing the reimbursement of medicines by the National Health Service (NHS). AIFA determines the reimbursement status of medicines based on their clinical and economic value and negotiates prices with pharmaceutical companies. Overall, AIFA plays a critical role in ensuring the safety and effectiveness of medicines in Italy, as well as managing the cost of healthcare through its reimbursement decisions. In the Leadiant and Aspen cases, we will see that, despite the fundamental role that AIFA plays, dominant pharmaceutical companies can nevertheless put in place abusive pricing strategies.

2.3 The role of Antitrust Authorities

Throughout history, the fundamental goal of antitrust laws has remained constant: safeguarding the competitive market process to serve the interests of consumers, by ensuring that businesses are

[5] Cupelli, A. (2018). *Funzioni dell'AIFA e ruolo nel contesto europeo*. [online] Available at: https://www.aifa.gov.it/documents/20142/1180150/2018-03-26_Funzioni_AIFA_e_ruolo_nel_contesto_europeo_Sapienza.pdf [Accessed 17 May 2023].

incentivized to operate productively, maintain reasonable pricing, and uphold high standards of quality. Antitrust Law is enforced, investigated, and managed by governmental authorities known as Antitrust Authorities. Each country has its own authority responsible for this task, in particular, the Italian competition regulator is the AGCM[6] (Autorità Garante della Concorrenza e del Mercato) that has the task of enforcing both Italian and European consumer protection laws. A self-governing agency, the Italian Competition Authority was created by Law No. 287 of 10 October 1990, also known as "The Competition and Fair Trading Act"[7], which introduced antitrust regulations in Italy. Additional powers were conferred to the authority through subsequent legislation, particularly in the areas of preventing unfair commercial practices, combating misleading and illegal comparative advertising, and enforcing conflict of interest regulations for government officials. As an independent Authority, it operates as a public agency whose decisions are taken on the basis of the Act without any potential interference by the Government. In the pharmaceutical industry, the AGCM has the power to investigate and sanction companies engaged in anti-competitive practices, such as abuse of dominant position, anti-competitive agreements, and collusion. In addition, the European Union also has its own Antitrust Authority, which is the largest and most active authority, alongside that of the United States.

i. Antitrust against excessive pricing in the Pharmaceutical Industry

In recent years, several competition enforcement actions against excessive pricing have taken place in the pharmaceutical sector, despite competition authorities usually being reluctant to intervene due to two challenging topics: actions against exploitive high prices and interventions in the pharmaceutical industry. Firstly, the traditional limited enforcement towards abuse of dominant position through excessive pricing practices poses a challenge to antitrust scrutiny over such conduct even if it is expressly prohibited by Article 102(a) of the Treaty on the Functioning of the European Union TFEU which states that: *"Any abuse by one or more undertakings of a dominant position within the internal market or in a substantial part of it shall be prohibited as incompatible with the internal market in so far as it may affect trade between Member States. Such abuse may, in particular, consist in (a) directly or indirectly imposing unfair purchase or selling prices or other unfair trading*

[6] en.agcm.it. (n.d.). *AGCM - Autorita' Garante della Concorrenza e del Mercato*. [online] Available at: https://en.agcm.it/en/about-us/.

[7] en.agcm.it. (n.d.). *AGCM - Autorita' Garante della Concorrenza e del Mercato*. [online] Available at: https://en.agcm.it/en/scope-of-activity/competition/mergers-and-acquisitions/foreword [Accessed 17 May 2023].

conditions"[8]. Additionally, the characteristics of pharmaceutical markets differ significantly from conventional competitive models, for this reason, they are highly regulated. The application of competition law against high prices in this sector requires a deep understanding of market dynamics and sector-specific regulations. Therefore, it may be appropriate to explore multiple intervention strategies, if possible, in cooperation with the relevant sector regulator, as well as the various regulatory measures that can be implemented to address high prices.

The main question is then to assess whether antitrust regulators are properly equipped to carry out cases effectively against high prices in this regulated sector where public agencies are in place by the government with the precise aim of providing an autonomous control on the market. Some argue that competition law should not intervene in the pricing field and rely on the market's self-correcting capability, in particular, high prices increase the profitability of a given market which attracts the entrance of new incumbents that will then reduce the market power of the dominant firms. In addition, some highlight that the practical difficulties in establishing the threshold of excessiveness may lead to enforcement errors. In fact, before intervention the regulatory body should also acknowledge and weigh the likelihood of both Type I errors (incorrectly identifying a problem) and Type II errors (failing to identify an existing issue). A Type II error would result from a competition authority failing to intervene against a pharmaceutical price that was, in reality, excessive. While, in Type I errors the authorities incorrectly identify a price as excessive. On the other hand, some favor antitrust intervention to protect consumer welfare. The latter view may be necessary in cases where the market cannot self-correct in a short timeframe. However, as outlined by the OECD guidance, bringing an antitrust case against exploitative excessive pricing requires stringent conditions, which, taken together, justify the intervention on an exceptional basis. The common conditions include significant market power of the entity imposing the high prices, the presence of substantial and enduring barriers to market entry, no adverse effects on research and development or innovation, and the impossibility of alternative regulatory intervention.

To date, the EU has primarily addressed excessive pricing cases regarding non-patented drugs that aren't adequately regulated by pricing frameworks. Generally, competition authorities have acknowledged the need to allow branded manufacturers to recover their investments during their exclusive period. However, public or government pressure may alter enforcement priorities, such as

[8] EUR-Lex - 12008E102 - EN. (2022). *Europa.eu*. [online] doi:http://europa.eu.int/eur-lex/lex/LexUriServ/LexUriServ.do?uri=CELEX:12008E102:EN:HTML.

a suggestion in a working paper by the former Chairman of the Dutch Competition Authority advocating for excessive pricing enforcement on patented pharmaceutical products[9]. Furthermore, the rise of personalized medicines and a greater emphasis by companies on orphan drugs puts higher pressure on antitrust authorities to rely on the principles of competition economics to address an issue that is primarily within the regulatory jurisdiction. Considering these factors, the subsequent chapters focus on two cases of excessive pricing practices (one regarding off-patent drugs), with which the AGCM antitrust authorities have recently dealt: Aspen and Leadiant. The analysis will be used to address the essential question concerning whether or not implementing competition policy is an appropriate approach for managing excessive pricing in the pharmaceutical industry.

ii. AGCM assessing abuse of dominant position in the pharmaceutical industry

The AGCM has the fundamental role of being the first to address the abuse of a dominant position through excessive pricing. Foremost, it will start a case investigation if there is a suspected breach of Article 102(a) (TFEU), which prohibits abusive conduct by companies that have a dominant position in a particular market. The case can originate either upon receipt of a complaint or through the opening of an *ex officio*[10] investigation or a sector inquiry. The first step in the investigation is to determine whether the undertaking concerned is dominant in any given market or not. To determine dominance the relevant market must be analyzed. Normally the product and geographic markets are defined. In particular, the product market is made of all the products and services that the consumer considers to be substitutes due to their characteristics, prices, and intended use.

In the pharmaceutical industry, the relevant product market is determined according to the therapeutic substitutability of the medicines. This relation of interchangeability is subdivided into therapeutic classes founded by the Anatomical Therapeutic Chemical classification system (ATC system). Pharmaceutical products are classified based on their main therapeutic use, following the principle that all products with similar formulations comparable in ingredients, unit dose, and method of administration, can have only one ATC code. However, the same active ingredient can receive more than one ATC code if there are clearly differentiated products for therapeutic indication, dosage, and

[9] Calcagno, C., Chapsal, A. and White, J. (2019). Economics of Excessive Pricing: An Application to the Pharmaceutical Industry. *Journal of European Competition Law & Practice*, 10(3), pp.166–171. doi:https://doi.org/10.1093/jeclap/lpy083.

[10] taxation-customs.ec.europa.eu. (n.d.). *What is VAT?* [online] Available at: https://taxation-customs.ec.europa.eu/what-vat_en#:~:text=The%20Value%20Added%20Tax%2C%20or.

method of administration. The classification is composed of five hierarchic levels. The 16 anatomical major groups are classified into the first and widest level (ATC 1) of therapeutic products. The second level (ATC 2) is a therapeutic or pharmacological group. The precise therapeutic indications of the pharmaceutical items are further grouped at the third level (ATC 3). Finally, the ATC4 level is the most detailed one, not available for all ATC 3, and refers for instance to the mode of action or any other subdivision of the group.

For what concerns the geographic market definition it is the area in which the conditions of competition for a given product are homogenous. In the pharmaceutical market, normally the scope of the competition is kept within the national dimension due to the institutional diversity that characterizes the health systems and pharmaceutical policies of each nation. If there are no close substitutes and the firm is found to hold a dominant position in the market, it is not in itself illegal. Nonetheless, a dominant enterprise bears a special responsibility to prevent any conduct that may impede fair competition. Such behaviors that may potentially constitute an abuse of dominance include: compelling consumers to purchase all units of a specific product solely from the dominant company (exclusive purchasing), establishing prices at a level that results in losses (predatory pricing), refusing to provide input necessary for competition in an auxiliary market, and charging excessive prices. The Authority can then require undertakings to provide all information necessary to an investigation via a simple request for information (RFI) or by decision and may take the case to judicial review. If the dominant firm abused its position by charging excessive pricing an analysis of the prices is made. But how can competition authorities define a price as excessive?

2.4 Can excessive pricing be defined?

The issue of excessive pricing in the pharmaceutical industry is complex and challenging, as it can be difficult to determine what constitutes unreasonable pricing. In economic terms, there are several factors that influence how prices are determined, with one important factor being the level of competition in the relevant market. In a highly competitive market, prices are typically set close to the cost of production. Conversely, markets with less competition tend to have higher prices. When a market is controlled by a monopoly, economic theory suggests that the monopolist will set prices to maximize profits. Prices that exceed this monopoly price would result in a loss of sales greater than the potential gain from the price increase. Thus, economic theory suggests that prices will not be raised above the monopoly price. Therefore, a prohibition against excessive prices seems unnecessary from an economic perspective because prices above the monopoly price are not rational and companies would be penalized for simply holding a dominant market position. It is thus not

surprising that the enforcement of excessive pricing remains limited around the world. Conceptually, excessive pricing has been underdeveloped and underused in practice for a long time. And it can be surprising that several cases have been undertaken in the pharmaceutical industry, in which monopoly rights are typically guaranteed by a patent, and it is necessary to consider the impact the antitrust intervention may have on the incentives to innovate. On the other hand, intervention against excessive pricing, especially for life-saving drugs, is fundamental to protect consumers' interests. Therefore, striking a balance between protecting consumers and promoting innovation is essential. The concept of excessive pricing remains important, and it is vital to continue exploring ways to address this issue also in the pharmaceutical industry.

i. The AGCM and the determination of excessive prices

If the undertaking is found to hold a dominant position, it is necessary to determine if it is abusing its market position through excessive pricing. To establish that a price is excessive under point (a) of Article 102 of TFEU it is necessary to demonstrate that the price charged by the dominant company has no reasonable relation to the economic value of the product supplied. According to the European Court of Justice (ECJ) this excess can, *inter alia*, be determined objectively if it is possible for it to be evaluated by seeing the difference between the product's selling price in question and its costs of production. For pharmaceutical companies, it is difficult to calculate all the manufacturing costs because it is hard to address all the indirect costs, for this reason, sometimes, some assumptions are made. Considering these factors, the ECJ have adopted a careful approach towards excessive pricing cases and, in United Brands, the EU Court has proposed a two-step evaluation test to determine excessive pricing: a dominant company's pricing must be both *excessive* and *unfair* ("in itself or when compared to competing products") to be considered illegal. Paragraph 252 of the ECJ ruling states that the key issues to be examined are whether there is an excessive gap between the actual costs incurred and the price charged, and if so, whether the price is unfair either on its own or in comparison to competing products. The ECJ recognizes that there may be alternative methods for determining whether a product's price is unfair, and that economic theorists have proposed several such methods.

The AGCM uses this two-stage test. For *excessiveness*, in some cases, the gross margin is first analyzed: AGCM considers first the contribution margin, the difference between *ex ante* prices and the direct costs of sales. Then the gross margin is calculated as the contribution margin in percentage of sales; and it is compared to the indirect costs in percentage of sales. If the price before the increase, already grants a contribution margin higher than the undertaking average and it is more than enough to cover overheads, then the price may be deemed excessive. A second analysis of price excessiveness

may be the cost plus, by comparing *ex-post* prices with a comprehensive measure of costs (direct costs + a portion of indirect costs + a reasonable profit margin). There is no clear analysis for *unfairness*, factors by which it can be addressed are, for example: inter-temporal comparison of prices, if there aren't economic justifications for price increases and lack of benefits for patients or NHS, also the nature of the drug plays an important role and the conduct of the undertaking during negotiations. If the undertaking charges both unfair and excessive prices, it is abusing its dominant position. Anyway, there is no clear analysis for the determination of excessiveness and unfairness, the United Brands two-stage test is used as a starting point but the choice of a methodology for the examinations and calculations is made accordingly to the case on hand.

3. The Aspen Case

3.1 Brief Introduction to the Aspen Case

As of September 2016, Aspen faced a fine of €5.2 million from the Italian Competition Authority (AGCM) for setting excessive and unfair prices on four crucial anticancer medications known as 'Cosmos.' These drugs were essential for certain patient groups who had no therapeutic alternatives, such as the elderly and children. The AGCM found that Aspen had abused its dominant position under Article 102(a) TFEU, which prohibits any abuse by single or multiple companies with a dominant market position within the internal market or a significant part of it that could potentially impact trade between Member States. Aspen obtained the trademark and marketing rights for Cosmos drugs from the originator, GlaxoSmithKline, in 2009, after the patent protection had expired, which allowed Aspen to establish a market niche for the life-saving treatment. To increase the prices and align them with those charged in other EU Member States, Aspen pursued an aggressive strategy towards the regulatory agency. AIFA agreed to a substantial upward revision of the prices of up to 1500% only after Aspen's threat to withdraw the drugs from the Italian market and make them available only through parallel trade from other European markets. The AGCM's investigation into this conduct began in 2014 and concluded with an infringement decision in 2016, establishing Aspen's dominant position in the relevant market as the only holder of the drugs and due to the lack of substitutability of those drugs. The AGCM evaluated the strategy of the generic-producing company using a two-step legal test based on the United Brands ruling by the Court of Justice of the European Union (CJEU). The investigation found Aspen's pricing strategy to be unfair and disproportionate, leading to the abuse of its right to price renegotiation by using aggressive bargaining tactics toward the sector regulator. In April 2018, Aspen and AIFA reached an agreement in which excessive prices were no longer applicable, and the AGCM did not impose an administrative fine. However, the European Commission initiated antitrust proceedings covering the European Economic Area other than Italy in May 2017, and the case marks the first investigation by the EU into anticompetitive conduct in the pharmaceutical industry.

3.2 Aspen's Case Analysis[11]

i. Premise

During 2014, there were reports of notable price increases for specific anti-tumor drugs sold by Aspen Pharma Trading Limited (APTL) in Italy. The Italian Medicines Agency AIFA provided information,

[11] L'AUTORITÀ GARANTE DELLA CONCORRENZA E DEL MERCATO. (n.d.). Available at: https://www.agcm.it/dotcmsDOC/allegati-news/A480_chiusura.pdf [Accessed 26 May 2023].

leading the Italian Competition Authority to launch an inquiry on November 19, 2014, into APTL and Aspen Italia S.r.l. (AI) to investigate potential violations of Article 102 of the Treaty on the Functioning of the European Union (TFEU). The Authority became aware of the price increases in July 2014 for the drugs owned by APTL and included in reimbursement classes A and H (covered by the SSN): Leukeran 2 mg - 25 tablets (chlorambucil), Alkeran 50 mg/10 mg powder and solvent for injection - 1 vial (melphalan), Alkeran 2 mg - 25 tablets (melphalan), Purinethol 50 mg - 25 tablets (mercaptopurine), and Tioguanine 40 mg - 25 tablets (thioguanine). These drugs' price increases were approved by AIFA on March 17, 2014, after negotiations with the company and ranged from approximately 300% to 1500% of the previous prices. (Shown in Figure 2). These increases were also reported by the consumer association Altroconsumo, as part of an investigation into the phenomenon of the "disappearance of drugs"[12] from the pharmaceutical distribution network. The Italian Competition Authority launched an investigation into these matters, better discussed in the subsequent sections.

Figure 2 Old and new prices of Aspen drugs in Italy (en.agcm.it)

Tabella n. 1: vecchi e nuovi prezzi farmaci Aspen in Italia

	Vecchio prezzo ex factory*	Nuovo prezzo ex factory	Vecchio prezzo al pubblico	Nuovo prezzo al pubblico	delta % prezzo al pubblico
Alkeran	€ 3,51	€ 57,62	€ 5,80	€ 95,10	1540%
Alkeran inj	€ 31,46	€ 149,87	€ 69,21	€ 247,35	257%
Leukeran	€ 4,54	€ 57,53	€ 7,50	€ 94,95	1166%
Purinethol	€ 10,19	€ 57,62	€ 16,82	€ 95,10	465%
Tioguanina	€ 32,71	€ 132,96	€ 53,99	€ 219,44	306%

*Per prezzo *ex factory* o *ex fabrica* si intende il prezzo del farmaco corrispondente al ricavo dell'industria, prima dell'aggiunta delle percentuali di spettanza della distribuzione farmaceutica. Al contrario, il prezzo al pubblico si ottiene appunto sommando al prezzo *ex factory* le percentuali di remunerazione dei soggetti della catena distributiva (grossisti e farmacisti).
Fonte dati: AIFA

ii. Aspen strategy in the regulatory classification of the drugs

In Italy, human medicines are classified based on their reimbursement status, which distinguishes between medicines reimbursed by the National Health Service (SSN) and those paid for by the

[12] www.altroconsumo.it. (n.d.). *Farmaci troppo cari: a Leadiant una sanzione di circa 3,5 milioni di euro per abuso di posizione dominante | Altroconsumo*. [online] Available at: https://www.altroconsumo.it/salute/farmaci/news/farmaci-cari-sanzione-antitrust [Accessed 17 May 2023].

patient. The classification of medicines is based on Article 8, paragraphs 10 and 14, of Law No. 537/1993 and subsequent amendments, which identifies the following reimbursement categories or classes:

a) Class A: essential medicines for chronic diseases, fully reimbursed by the SSN. These medicines are provided by direct distribution through territorial pharmacies or public health facilities.

b) Class H: medicines for hospital use, reimbursed by the SSN and used in hospitals or health facilities.

c) Class C: medicines entirely paid for by the patient. Within Class C, a distinction is made between medicines with a medical prescription requirement and those without.

The price of Class A and H medicines is fully reimbursed by the SSN when they are covered by a patent or when there is no generic or equivalent drug available on the market. For off-patent drugs in Class A, whether they are originator drugs or their generics, the SSN reimburses the lowest price among equivalent drugs on the market (the so-called reference price). The prices of Class C medicines are freely determined by the manufacturers and paid entirely by the patient. AIFA monitors the prices of prescription-only Class C medicines, which can only be increased every two years and with increases not exceeding the planned inflation rate. For non-prescription Class C medicines, the price is freely determined by the manufacturer. The retail price of a medicine in any reimbursement class is obtained by adding the ex-factory price, also known as the ex-factory value, to the VAT[13] and the wholesaler's and pharmacist's shares, as determined by law.

For all medicines belonging to the classes A or H, the price of the reimbursed drugs by the State is determined through a bargaining process between AIFA and the undertaking. According to Article 6 of the Delibera CIPE "In the negotiation process, the parties represented by the company and the administration must, for the purposes of defining the price, accompany their proposals with adequate economic assessments of the product and the industrial context (with reference to investments in production, research and development and exports), market and competition in which the same product is placed. The negotiation procedure concludes in the event of an agreement between the parties with the fixing of a price […] In the event that an agreement on the price is not reached, the product will be classified in range C referred to in paragraph 10 of the art. 8, of the law of 24 December 1993, n. 537." Aspen requested, immediately after the price set by AIFA, a reclassification of the drugs to class C: drugs at the expense of the patient. AIFA added to this request that it " was a totally exceptional circumstance: in fact, it is the first case ever occurred for anticancer drugs, given

[13] taxation-customs.ec.europa.eu. (n.d.). *What is VAT?* [online] Available at: https://taxation-customs.ec.europa.eu/what-vat_en#:~:text=The%20Value%20Added%20Tax%2C%20or.

their life-saving nature and irreplaceability, as certified by expert haematologists […] and that it undoubtedly represents an aggressive behavior of the company in the negotiation with AIFA". Consequently, the CTS (Commisione Tecinico Scientifica) of AIFA, answered to the appeal for reclassification in level C by asking the company to formulate a price proposal that allows it to keep the drug under reimbursement by the SSN. To this Aspen prosed a significant increase in prices for the drugs, not sustainable for the SSN, and threaten to withdraw the drug form the Italian Market if approval to direct reclassification to class C of the drugs was not provided. The negotiation was then concluded with the price increase determined by Aspen.

iii. The relevant market

In the Aspen case, the relevant markets under consideration were pharmaceutical products containing the active ingredients melphalan, chlorambucil, tioguanine, and mercaptopurine. In the pharmaceutical sector, defining the relevant market typically involves identifying therapeutic classes based on the chemical action and therapeutic purpose of the drug. The ATC divides drugs according to a five-level alphanumeric classification system. The ATC3 is the third level of the classification and identifies a pharmacological therapeutic subgroup to which drugs are usually intended to treat the same diseases and are generally interchangeable with each other but not with those belonging to other classes at the first and second levels. ATC3 is therefore the starting point for identifying substitutable products for the purpose of defining the relevant market. However, it is often necessary to conduct a specific substitutability analysis based on economic and behavioral considerations typical of antitrust analyses, which may lead to surpassing the ATC3 level when "competitive constraints" between the relevant companies are found at a different level of the ATC classification or according to different grouping criteria of drugs. Depending on the circumstances of the case, as clarified by the European Commission, even considerations related to the prescribing or reimbursement methods for drugs, and the general organization of supply and demand may assume even greater importance. In any case, the definition of antitrust markets cannot ignore preliminary medical evaluations regarding the therapeutic substitutability of products, as it is essential that the products being compared from an economic perspective are considered therapeutically substitutable by the competent scientific bodies and the scientific community.

In the Aspen case, the drugs under consideration were antineoplastic agents (ATC2, L01), used in hematology to treat, for example, leukemias, lymphomas, myelomas, in certain stages of the treatment of these diseases. They belonged to two different chemical therapeutic subgroups, ATC3 level:

Leukeran and Alkeran were alkylating agents (ATC3, L01A) while Purinethol and Tioguanine were antimetabolites (ATC3, L01B). Specifically, Leukeran and Alkeran were "nitrogen mustard analogs" (ATC4, L01AA), while Purinethol and Tioguanine were "purine analogs" (ATC4, L01BB). Each medicinal product considered contained a different active ingredient at the ATC5 level. For each of the Aspen drugs, despite the expiration of relevant patents, none of the Aspen drugs had direct substitutes or generic versions available on the market, as there were no other products on the market containing the same molecule. AIFA and GIMEMA[14], an independent hematologists group, consulted experts who acknowledged that drugs produced by other pharmaceutical companies for similar indications couldn't replace Aspen's drugs, which were used in specific patient populations and treatment phases where no alternative drugs were available. Purinethol and Tioguanina are primarily used to treat acute lymphoblastic leukemia (ALL) in both children and elderly patients, while Leukeran is used to treat chronic lymphocytic leukemia (CLL) in elderly patients and some forms of non-Hodgkin's lymphoma. Alkeran is mainly used to treat multiple myeloma and is a component of some advanced protocols in combination with other anticancer drugs. The experts indicated that Aspen's drugs were still widely used and considered irreplaceable for these diseases that typically affect vulnerable patients, including children, elderly patients, and weak patients who are particularly sensitive to cancer therapy's side effects. GIMEMA also confirmed that Aspen's drugs have a low level of toxicity and are highly tolerated as they have no significant side effects due to their long-standing use in treating leukemia. Additionally, these drugs were included in the A reimbursement category and distributed in tables, allowing for their distribution through local pharmacies and use in home maintenance therapy for both chronic and naïve patients.

While Aspen's drugs could appear disused and surpassed by new treatments for some authorized therapeutic indications, they remained critical for the diseases mentioned above. Experts agree that the Leukeran drug is the standard treatment for chronic lymphocytic leukemia (CLL) and is particularly useful for elderly patients who are unable to tolerate more aggressive treatments. The introduction of a new drug, Zydelig, which was authorized for use in Italy but was subject to additional monitoring due to safety concerns, could have potentially reduce the use of Leukeran. However, experts noted that there were no accepted substitutes for Leukeran, and that it was irreplaceable in certain essential treatment protocols. Similarly, the Alkeran drug was primarily used in the treatment of multiple myeloma, a cancer that is typically diagnosed in patients between the ages of 75 and 79. Experts noted that Alkeran was irreplaceable and that there were no other drugs

[14] Fondazione Gimema. (2023). *Fondazione Gimema – Franco Mandelli onlus*. [online] Available at: https://www.gimema.it [Accessed 17 May 2023].

that had been shown to be as effective in certain treatment settings. Furthermore, Aspen and GSK, the previous holder of the drugs' marketing authorization, had both claimed that the drugs were essential and had no therapeutic alternatives. Purinethol is an important drug in the treatment of acute lymphoblastic leukemia (ALL) and is considered indispensable for the treatment of children, as ALL is the most common cancer in childhood. Aspen also claimed that each of the drugs in question was unique in its therapeutic category and had no alternative treatments in Italy. Experts agreed that the drugs in question had a different toxicity profile than other drugs in their therapeutic category, making them suitable for use in elderly and pediatric patients who cannot tolerate more toxic treatments. The drugs' oral formulation also made them suitable for use in maintenance therapy, which can last for many years. The drugs' inclusion in the Italian national health system's (SSN) reimbursement list, along with the absence of therapeutic alternatives, made them essential treatments that couldn't be substituted with other drugs. The relevant market for each drug was limited to the national territory of Italy, as the pharmaceutical market is traditionally considered to be national due to differences in healthcare policies and access regimes. Aspen held a monopoly on each of the drugs in question, and the size of the relevant markets was relatively small, with a combined annual turnover of approximately [5-10] million euros.

iv. Price Analysis: excessiveness and unfairness

This section aims at analyzing the prices applied by Aspen for Cosmos drugs. In particular, the methodologies applied to determine how the prices charged by the undertaking in its dominant position were considered abusive as the group exploited its market position to obtain commercial advantages, by applying excessive pricing without any reasonable relationship with the economic value of the service provided. Foremost the economic value of the good has to be determined. Lacking a regulatory framework, it must reflect a measure of the production costs borne by the company to realize the good. The analysis of the prices was conducted through a two-phase procedure, the first of which assesses whether there is an *excessive pricing* disproportion between the cost of production and the actual price requested by the company. If this disproportion is found to be positive, the second phase will aim to determine whether an *unfair price* was imposed, considering various elements specific to the case.

A. Excessive prices

The disproportion of the price imposed is assessed by referring to the total costs borne by the undertaking for realizing the product, including, first, variable direct costs, which are expressed as

COGS (cost of goods sold), then a quota of fixed direct costs, and a quota of indirect costs deemed reasonably related to the production of the good under examination. It is also reasonable to include a fair remuneration for the activity carried out, in addition to the total costs borne by the undertaking for realizing the product. Indicators of the undertaking's profitability, such as ROI, ROE, ROCE, WACC, sales profitability rates, and contribution margin, can be considered. To determine whether a price is considered abusive, there are no fixed quantitative thresholds or precise mathematical relationships that can define the level of disproportion between prices and costs. According to the economic doctrine and jurisprudence on excessive pricing, which suggests that the use of multiple calculation and analysis methodologies is preferable since there is no regulatory framework for defining the abusiveness of the prices imposed, two methodologies of analysis were used to evaluate the disproportion between prices and total costs in the case at hand. The first involved analyzing the disproportion between prices and costs measured through the *gross contribution margin* of each single Cosmos drug, and the second examined the disproportion between the prices applied and the costs borne by Aspen measuring the difference between profits and the so-called *cost plus*. The prices taken into consideration for the calculation are to be considered net of discounts imposed by law and of the distribution margin recognized by Aspen to its distributor, LFM[7]. The hypotheses on which the economic analysis is based were favorable to the undertaking, and the analysis was conducted using several calculation and analysis methodologies, which were viewed favorably in the economic doctrine and jurisprudence concerning excessive pricing. Figure 3 shows an extrapolation of the data present in APHL's[8] financial statement, which will be used in the analysis that follows.

[7] Anon, (n.d.). *Laboratorio Farmacologico Milanese | LFM*. [online] Available at: https://lfm.it/ [Accessed 17 May 2023].

[8] Anon, (n.d.). *About Aspen – Aspen Pharmacare*. [online] Available at: https://www.aspenpharma.com/about-aspen/.

Figure 3 Consolidated financial statement APHL (en.agcm.it)

Tabella n. 4: Dati di bilancio consolidato APHL (valori in milioni di €)*

	BILANCIO CONSOLIDATO APHL	Giu-2014	Giu-2015
PQ	RICAVI	2.079	2.654
CDQ	COSTI DIRETTI (COSTO DEL VENDUTO)	(1.112)	(1.387)
PQ - CDQ = MC	**MARGINE DI CONTRIBUZIONE**	**966**	**1.268**
a)	SELLING AND DISTRIBUTION EXPENSES	(310)	(413)
b)	ADMINISTRATIVE EXPENSES	(116)	(207)
c)	OTHER OPERATING EXPENSES	(66)	(67)
d)	OTHER OPERATING INCOME	49	40
MOL = MC – a) - b) - c) +d)	**MARGINE OPERATIVO LORDO**	**523**	**621**
e)	INVESTMENT INCOME	20	28
f)	FINANCING COSTS	(95)	(169)
PROFIT prima delle imposte = MOL + e) – f)	**RISULTATO PRIMA DELLE IMPOSTE**	**448**	**480**

Fonte: *Annual financial statement* 2014 e 2015 APHL
* I bilanci di APHL sono valorizzati in rand sudafricano (ZAR). Sono stati applicati a tali valori i tassi di cambio ZAR/€ indicati dal gruppo Aspen nel proprio *integrated report.*

Contribution Margin Analysis

1) Methodology

We now analyze the first methodology which assesses the disproportion between prices and costs by measuring it through the gross contribution margin provided by each product. This is done by comparing the margin to the total fixed and indirect costs that Aspen incurs, as shown in APHL's financial statement. The contribution margin of each Cosmos drug is determined using the following formula:

PQ - CDQ = MC

Where:

- P = unit price
- Q = quantity
- CD = unit direct cost
- MC = contribution margin

The single Cosmos product's profits (PQ) minus the direct cost attributed to it (CDQ), which is equal to the COGS, results in a contribution margin to the net business income (MC). This margin is calculated as a percentage of sales from APHL's financial statement, MC%, ranging from 30% to 70% of sales, and is compared with the indirect costs also in the percentage of sales, CI%, equal to 30% of sales, to establish the excessive marginality guaranteed by each Cosmos product.

MC% - CI% = EXC

Where:

- CI = indirect costs
- EXC = excess

2) Application to the Aspen Case

Before analyzing the profitability of individual Cosmos products, it is essential to note that these products collectively generated a positive contribution to Aspen's income even before the renegotiation of prices, as measured by the gross contribution margin. In 2009, Glaxo and Aspen's Sales and Distribution agreement indicated that Cosmos products globally produced a total gross margin of around [1-50] million euros. For the Italian market, the set of five drugs under examination produced a gross margin of approximately [600,000-700,000] euros. The acquired spreadsheets during inspections at Aspen Pharma Ireland Limited (APIL) reveal the Profit and Loss Account data (P&L) of each relevant product, which can be filtered for each national market. From which is evicted, specifically for Italy, that Cosmos drugs produced a positive contribution margin equal to at least [20-30]% of the sales value.

Figure 4 Exhibits an extrapolation of the data, specifically the sales value or sales profit (PQ), cost of goods sold (COGS) related to direct costs (CDQ), and the resulting contribution margin (gross profit) of the products that were examined. This is in reference to the year 2013 and the Italian market. Additionally, the lower section of the table presents the analysis of the profitability ratios of the products, which includes the gross profit percentage and the COGS percentage.

Figure 4 Analytical accounting: contribution margin of Aspen's product before the renegotiation (en.agcm.it)

Table n. 5 – Analytical accounting: contribution margin of Aspen's products before the renegotiation

Valori in € 000				
MERCATO	**ITALIA**		**ANNO 2013**	
PRODOTTO	ALKERAN / MELPHALAN	LANVIS / THIOGUANINE	LEUKERAN / CHLORAMBUCIL	PURINETHOL / MERCAPTOPURINE
RICAVI DI VENDITA	[200-250]	[60-70]	[90-100]	[200-250]
COSTO DEL VENDUTO (COGS)	[(50-100)]	[(1-50)]	[(50-100)]	[(50-100)]
MARGINE LORDO DI CONTRIBUZIONE (GROSS PROFIT)	[100-150]	[1-50]	[1-50]	[100-150]
RATIO ANALYSIS				
GROSS PROFIT %	[50-60]%	[30-40]%	[20-30]%	[60-70]%
COGS %	[40-50]%	[60-70]%	[70-80]%	[30-40]%

Based on this information of the year 2013, therefore referring to the prices prior to the renegotiation discussed here, the contribution margin for the business income of the drugs under examination, MC%, ranged between [20-30]% for Leukeran and approximately [70-80]% for Purinethol. As a result, the cost of sales expressed as a percentage of sales, CD%, was between [70-80]% and [30-40]%. Comparing this information with Aspen's financial statements closed in June 2014 reveals two

key points. First, the profitability of Aspen's products in Italy was, on average, in line with the profitability generated by the entire group's activity. Second, none of the Cosmos products generated a contribution below the sales value. Consequently, the products under investigation in 2013 contributed to the net income of the Aspen group between [20-30]% and [70-80]%, or, symmetrically, entailed costs of goods sold not above [70-80]% of sales. This was in line with the average contribution sales values resulting from the group's last financial statement before the price increase under examination and consistent with a positive net income for the fiscal year. The conclusions above can be formalized as follows. For each Cosmos product in 2013:
MCi % ≥ [20-30]%

Given the measure of indirect costs expressed as a percentage of the group's sales equal to 30%, each product assured at least a balance between profits and total costs, even before the price increase under discussion: EXC = MCi % - CI% ≥ 0
The measure of indirect costs identified above also includes the balance of capital management and taxes since 30% corresponds to the difference between the gross contribution margin and the net income of the fiscal year, already cleared from interests and taxes. In conclusion, the analysis implies that the prices of Cosmos drugs applied by Aspen in Italy, even before the negotiation with AIFA, were above the economic value of the products, calculated according to the total direct and indirect costs borne by Aspen for their realization. This means that after the increases decided by AIFA, from 300% to 1,500%, were applied to the sales profits of Cosmos drugs in March 2014, Aspen's profits from selling Cosmos drugs in Italy significantly exceeded the total costs attributable to the products under examination, at least in equal percentage.

Analysis of the profits and total costs of the Cosmos drugs

1) Methodology

In the second methodology proposed for analyzing excessive pricing in the pharmaceutical industry, the disproportion between the prices charged and the costs incurred by Aspen for Cosmos drugs is examined using the following formula:

Excess (EXC) = Price x Quantity (PQ) - (Direct Costs x Quantity (CDQ) + α * Indirect Costs (CI) + Return on Sales (ROS))

Here, the term in parentheses is called "cost plus," which is the sum of direct costs, the portion of indirect costs attributable to the product, and the return on sales.

cost plus = (CDQ + αCI + ROS) therefore: PQ – cost plus = EXC.

The resulting excess is then evaluated for possible unreasonableness. The excess measure is compared to cost plus to obtain a percentage value (EXC%), which is invariant to sales volume and comparable to other cases of excessive pricing.

2) Application to the Aspen Case

In applying this methodology to the specific case, several assumptions are made to protect the interests of the party involved. First, the antitrust authorities choose to get the indirect costs, to be attributed pro-quota, from the holding's consolidated financial statements. As previously mentioned, the company needs to consider not only the direct costs of production but also a portion of the operating expenses that cannot be fully attributed to the product due to their horizontal nature. To determine the proportion of costs compared to the economic value of the product, competition authorities have the discretion to identify indirect costs to allocate to individual products based on a "case-by-case" assessment.

In this case, the company chose to allocate indirect costs to Cosmos products based on the consolidated financial statements of the South-African holding APHL, as the Italian turnovers for the drugs are registered by the company AH in Dubai. This choice was made because, as the Party clarified, Aspen uses a *buy and sell* distribution model for selling Cosmos products in Italy. This involves transferring the products to an independent Italian distributor, which then assumes ownership of the products. For this reason, the European undertakings APIL, APTL and AI do not carry out a direct activity connected to the selling and distribution of Cosmos drugs on the Italian territory so it would be incorrect to allocate indirect costs to those entities. Furthermore, the decision to allocate indirect costs to the Italian market from the holding's financial statements protects the company as it includes a portion of all indirect costs incurred by the Aspen group for its overall business. The second assumption was made for the determination of the allocation coefficient of indirect costs. After the indirect costs that need to be ascribed to each Cosmos product have been identified, it is important to establish an allocation principle, which determines which portion of the indirect costs can be attributed to the production of each individual drug. This allocation principle is essential in determining the economic value of each drug. The chosen criterion used the cost of goods sold as the allocation "driver" of indirect costs. This means that the indirect costs identified in APHL's financial statements will be allocated to Cosmos products for Italy based on a ratio derived from the relationship between the specific cost of goods sold for each Cosmos drug in the Italian market and the total cost of goods sold in the holding company's financial statements. This ratio, called α, is

multiplied by the items of indirect costs from the same financial statements to obtain the portion of those costs to be attributed to individual Cosmos drugs in the Italian market. This choice is justified by two reasons: (i) it seems reasonable to assume that a company's indirect costs affect individual products in proportion to direct costs, and (ii) direct costs incurred for the production of a good appear to be the best proxy for the inputs necessary for its realization, and therefore, the best suitable criteria for pro quota allocation of indirect costs to that product. For each Cosmos product, the allocation coefficient is determined as follows:

αi = COGS Product (i) Italy / total COGS group

The portion of the total indirect costs to be attributed to the drug (i) is then determined using the following formula:

CIi = αi (total CI group)

The financial statement items allocated include "Selling and Distribution," "Administrative expenses," and "Other Operating Expenses," which represent all indirect operating costs. Subtracting these costs from the gross contribution margin results in the operating management, or EBIT (Earnings before interests, taxes, depreciation, and amortization). The third assumption was made on the remuneration rate for the business activity. The analysis of the disproportion between prices and costs borne by a dominant undertaking to establish excessive prices must consider a profitability margin for the company. It is reasonable for a company to expect a fair remuneration for its activity through the price applied for a specific product. Therefore, a profitability measure was added to the set of direct and indirect costs attributable to the product (CDQi + αi CI). While various profitability indexes can be identified, the Return on Sales (ROS) was chosen over capital remuneration indexes for Aspen, as it is a pharmaceutical group mainly involved in commercializing generic and branded drugs developed by other companies. As a consequence, Aspen has limited investments in research and development activities, particularly for Cosmos drugs. In fact, since they are not produced by Aspen, the company does not possess tangible assets related to the production of these drugs. The activities carried out by the Aspen group in commercializing Cosmos drugs in Italy are limited to ordering, stocking, and transferring the products to the external distributor, which does not require significant investments in tangible assets. Therefore, a measure of sales profitability is the most significant index to examine the remuneration of these products in the Italian market. In this case, a ROS of 13% was granted, which corresponds to the average return on sales rate realized by the two major pharmaceutical companies active in the production of generic drugs worldwide in the two-year period 2013-2014. The last assumption was made on the ex-post analysis. To clarify the

methodology used, the excessive pricing analysis for Cosmos products was conducted using internal accounting data from 2013, which includes the specific profits, cost of goods sold and contribution margin for each product line (Alkeran, Leukeran, Purinethol, and Tioguanine) related to various markets, including Italy, from 2009 to 2013. The analysis aimed to examine the disproportion between prices and costs of Cosmos products for the Italian market, and the cost-plus values for each product line were determined for the year before the price increases decided by AIFA. As there was no analogous set of internal data available for the period following the price increases in Italy, the ex-post profitability of Cosmos drugs was analyzed by applying the following increases to the 2013 costs and profits values: first, the sales profits were increased according to the price increase percentages established by AIFA's resolution of March 2014, second, assuming constancy of sales volumes, the direct cost items were increased by 25%, which is the proportion of the costs of Aspen's entire group, based on a comparison between the consolidated financial statements of the first fiscal year following the price increases of June 2015 and the last financial statements before the increases of June 2014. This assumption is favorable for the company since the cost of sales of Cosmos drugs had a constant trend between 2009 and 2013, not justifying any increase between 2013 and 2014. Third the indirect cost items to ascribe to the single Cosmos products for the Italian market were based on data present in the group's first financial statements following the price increases examined, which is the financial statement of the fiscal year closed in June 2015.

The analysis of the "cost plus" to determine the disparity between prices and costs.

The cost-plus analysis which involves calculating the operating margin plus a reasonable remuneration of the business activity, was used to determine the disproportion of prices compared to costs for each Cosmos product. Figure 5 displays the profit and loss account of each product *before price increases*, highlighting the contribution margin and the operating margin. The results come from the difference between the specific turnovers, direct costs, and total indirect costs of each product. The attribution of indirect costs to a single product is based on the allocation coefficient α. Whereas the entry *"Other operating expenses"* stands for all the costs associated with Aspen's purchasing of the marketing rights of the products. In fact, the acquisition of the trademarks was not included in the direct costs. The Party quantify the costs to be between 300 and 400 million globally but didn't have a breakdown of this cost per product or country. As a result, this cost is accounted for in the profit and loss statement of Cosmos products as a proportion of the holding's indirect costs assigned to each individual drug.

Figure 5 Income statement Cosmos products 2013 (en.agcm.it)

Tabella n. 6 - Conto economico prodotti Cosmos 2013 (valori in €)					
DESCRIZIONE	FORMULA	PURINETHOL	LEUKERAN	ALKERAN	TIOGUANINA
Ricavi specifici	PQ_i	[200.000-250.000]	[90.000-100.000]	[200.000-250.000]	[60.000-70.000]
Costi diretti specifici	CDQ_i	[60.000-70.000]	[70.000-80.000]	[90.000-100.000]	[30.000-40.000]
Margine di contribuzione lorda	**MC_i = PQi - CDQi**				
chiave di allocazione costi indiretti	α_i = CDQi / CDQ totali	[0-0,010%]	[0-0,010]	[0-0,010%]	[0-0,010%]
Allocazione costi indiretti	$CI_i = \alpha_i$ x CI totali				
	- Selling and distribution	[10.000-20.000]	[10.000-20.000]	[20.000-30.000]	[10.000-20.000]
	- Administrative expenses	[5.000-10.000]	[5.000-10.000]	[10.000-20.000]	[5.000-10.000]
	- Other operating expenses	[0-5.000]	[0-5.000]	[5.000-10.000]	[0-5.000]
Margine operativo	**$EBIT_i = MC_i - CI_i$**	[100.000-150.000]	- [0-5000]	[70.000-80.000]	[5.000-10.000]
fonte: elaborazioni Agcm su dati dell'impresa					

Figure 6 represents the profit and loss account of each product *after price increases*, the ex-post revenues, and direct and indirect costs were allocated following the assumption previously discussed. Indirect costs were determined as a quota of the total indirect costs of the first APHL financial statement after the negotiation for the price increase. The revenues were increased according to the 300% and 1500% of the price increase. Consequently, the direct costs were calculated by adding to the ex-ante costs the percentage increase of the costs from 2014 and 2015.

Figure 6 Income Statement Cosmos products ex-post (en.agcm.it)

Tabella n. 7 - Conto economico prodotti Cosmos *ex post* (valori in €)					
DESCRIZIONE	FORMULA	PURINETHOL	LEUKERAN	ALKERAN	TIOGUANINA
Ricavi specifici dopo l'aumento	PQ_i *ex post* = PQi x (1+ΔP%)	[1.100.000-1.200.000]	[1.200.000-1.300.000]	[2.200.000-2.300.000]	[200.000-250.000]
Costi diretti specifici dopo l'aumento	CDQ_i *ex post* = CDQi x (1 + ΔCD totali %)	[70.000-80.000]	[80.000-90.000]	[100.000-150.000]	[40.000-50.000]
Margine di contribuzione lorda dopo l'aumento	**Mci *ex post* = PQi *ex post* - CDQi *ex post***	[1.000.000-1.100.000]	[1.100.000-1.200.000]	[2.100.000-2.200.000]	[150.000-200.000]
chiave di allocazione costi indiretti	α_i = CDQi / CDQ totali	[0-0,010%]	[0-0,010%]	[0-0,010%]	[0-0,010%]
Allocazione costi indiretti dopo l'aumento	CI_i *ex post* = α_i x CI totali *ex post*				
	- Selling and distribution	[20.000-30.000]	[20.000 -30.000]	[30.000-40.000]	[10.000-20.000]
	- Administrative expenses	[10.000-20.000]	[10.000-20.000]	[10.000-20.000]	[0-10.000]
	- Other operating expenses	[0-5.000]	[0-5.000]	[5.000-10.000]	[0-5.000]
Margine operativo dopo l'aumento	**$EBIT_i$ *ex post* = MC_i *ex post* - Cii *ex post***	[1.000.000-1.100.000]	[1.100.000-1.200.000]	[2.100.000-2.200.000]	[150.000-200.000]
fonte: elaborazioni Agcm su dati dell'impresa					

Figure 7 displays the cost plus for each Cosmos product before and after price increases. The cost plus is calculated by adding up direct costs, the quota of indirect costs, and remuneration for the company's activity measured by a Return on Sales equal to 13%, in line with the average results achieved by the two major companies of generic drugs worldwide.

cost plus i = CDQi + αi CI + ROSi

Figure 7 Determination of the cost plus before and after the prices increase (en.agcm.it)

Tabella n. 8 - Determinazione del *cost plus* prima e dopo gli aumenti di prezzo (valori in €)

DESCRIZIONE	FORMULA	PURINETHOL	LEUKERAN	ALKERAN	TIOGUANINA
Return on sales 2013	ROS 2013 = ROS 13% x PQi	[20-000-30.000]	[10.000-20.000]	[20-000-30.000]	[0-10.000]
Return on sales *ex post*	ROS *ex post* = ROS 13% x PQi ex post	[100.000-150.000]	[150.000-200.000]	[250.000-300.000]	[30.000-40.000]
cost plus 2013	**CDQi + α_i CI + ROS 2013**	**[100.000-150.000]**	**[100.000-150.000]**	**[150.000-200.000]**	**[60.000-70.000]**
cost plus ex post	**CDQ_i *ex post* + α_i CI_i *ex post* + ROS *ex post***	**[250.000-300.000]**	**[250.000-300.000]**	**[450.000-500.000]**	**[90.000-100.000]**

fonte: elaborazioni Agcm su dati dell'impresa

Then the excess of profits over cost-plus is processed for each drug before and after price increases, and the results are shown in Figure 8. EXC=PQ-cost plus

The Figure also shows the difference in revenues and costs as a percentage of the cost plus, allowing for the comparison with various analyses of price unfairness carried out in previous cases.

EXC % = EXC/cost plus %

Figure 8 Determination of the excess on the cost plus before and after the increase in prices (en.agcm.it)

Tabella n. 9 - Determinazione dell'eccesso sul *cost plus* prima e dopo gli aumenti di prezzo (valori in €)

DESCRIZIONE	FORMULA	PURINETHOL	LEUKERAN	ALKERAN	TIOGUANINA
Eccesso dei prezzi sul *cost plus* prima degli aumenti	**PQ_i – *cost plus* = EXC_i**	[80.000-90.000]	[da -10.000 a -20.000]	[50.000-60.000]	[da -200 a -300]
Eccesso dei prezzi sul *cost plus* dopo gli aumenti	**PQ_i *ex post* – *cost plus ex post* = EXC_i *ex post***	[850.000-900.000]	[950.000-1.000.000]	[1.800.000-1.900.000]	[100.000-150.000]
Eccesso in percentuale del *cost plus* prima degli aumenti	**EXC_i % = EXC_i / cost plus $_i$**	[70-80%]	[da -20 a - 10%]	[20-30%]	[da -5 a 0%]
Eccesso in percentuale del *cost plus* dopo gli aumenti	**EXC_i % *ex post* = EXC_i *ex post* / cost plus $_i$ *ex post***	**[300-350%]**	**[300-350%]**	**[350-400%]**	**[100-150%]**

fonte: elaborazioni Agcm su dati dell'impresa

The analysis concludes that even before the application of new prices, Aspen registered a high difference between profits and total costs for some Cosmos products, with a profit-cost difference

between 20-30% and 70-80%, factoring in a 13% return on sales. The new prices applied by Aspen in Italy produced a relevant gap of profits over costs, which shows a significant increase in the excess as a percentage of the cost-plus with values ranging from [100-150]% to [350-400]% for the realization of single drugs, including a reasonable remuneration margin. Furthermore, Aspen's investments in trademarks were included as indirect costs in the analysis, despite not being considered necessary. The study also examined an alternative hypothesis where the trademark costs from GSK were treated as fixed direct costs. This alternative did not significantly change the conclusions regarding the disproportion between prices and costs. The costs for purchasing Cosmos trademarks were estimated for the Italian market based on limited information from the party involved. Aspen stated that the amount paid to purchase the trademarks was four times the profits made at the time of purchase. The expense was estimated for each drug in the Italian market in 2009. An annual amortization quota was calculated based on an estimated 20-year useful life for the drugs. This aligned with Aspen's accounting policies and the drugs' lasting therapeutic value. The analysis showed that even under this alternative hypothesis, the excess percentages remained high, ranging from 100-150% to 300-350%.

B. Unfair prices

1) *Methodology*

It is also important to consider that in Aspen's case, given the peculiar nature of the products under examination, which are life-saving drugs, the determination of their value cannot be carried out taking into consideration consumers' willingness to pay. The willingness to pay for life-saving drugs lacking therapeutic alternatives can only tend towards infinity, potentially justifying any price increase. For this reason, in the second phase of the analysis, any qualitative elements that are not directly reflected in the production costs used to calculate the price-cost disproportion and are specific to the case being examined shall be evaluated. In fact, the assessment of the unfairness of the prices imposed is to be carried out keeping into account the circumstances of the actual case and the absence of "reasonableness" in the relationship between price and economic value of the product, in the light of the specificities of the case, considering possible elements capable of affecting the total value of the service provided. The analysis takes into consideration various elements, including a comparison between the prices imposed by the undertaking and prices applied previously or in other markets, demand qualitative factors not directly reflected in the costs borne by the undertaking, the presence or absence of economic justifications for the price levels imposed, the presence of potential competitive pressure, the nature of the product, and the undertaking's characteristics.

2)*Application to the Aspen's Case*

The excessive pricing analysis, based on two distinct calculation methods, revealed how the new prices set by Aspen after renegotiating with AIFA were disproportionate compared to the company's actual costs. The second step of the test is to determine if these prices were "unreasonable" with respect to the economic value of the provided service and thus unfair according to Article 102, letter a) of the TFEU, considering the specific case. considered the previously cited factors were considered in evaluating the price unfairness, including:

- Comparing new and old prices: The analysis of price evolution over time is particularly relevant due to the irreplaceability of Cosmos drugs with other authorized products in Italy, making it impossible to compare prices with competing drugs. Additionally, the differences in healthcare systems and pharmaceutical regulations among European Union countries and the pan-European price increase strategy make a comparison with prices in other national markets insignificant. The comparison between new and old prices is important as the original prices were applied without modifications by the previous marketing authorization, AIC[9], holders since the first introduction of Cosmos drugs in the market. AIFA considers the need to remunerate the research activity borne by the company for the realization of the drug, with initial prices set to recover the costs of discovering and developing the product. The Party's objection that the price increases are justified due to inflation is invalid as the initial prices were already suitable for covering the marginal costs necessary for production and commercialization. Organizational differences between Aspen and GSK do not justify the different price policies as the initial prices were suitable for ensuring a positive margin for the company.
- Lack of economic justifications for the substantial increase: Aspen did not conduct any cost evaluations in setting the negotiation strategy or during the negotiation with AIFA. The company's references to costs are unsupported by any analysis or data. Furthermore, the increases in medical-scientific promotion costs that the undertaking needed to recover are unnecessary as the drugs under examination are already well-known, same applies to the costs for pharmacovigilance and compliance with GMP[15] standards which involve the entire

[9] aifa.gov.it. (n.d.). *Autorizzazione dei farmaci*. [online] Available at: https://www.aifa.gov.it/autorizzazione-dei-farmaci# [Accessed 17 May 2023].

[15] European Medicines Agency (2018). *Good manufacturing practice - European Medicines Agency*. [online] European Medicines Agency. Available at: https://www.ema.europa.eu/en/human-regulatory/research-development/compliance/good-manufacturing-practice.

pharmaceutical production and not specifically Aspen's drugs, moreover, the standards are applied to the manufacturer of the product, consequently not directly to the undertaking. In addition, the disproportion of the new prices was established over a total cost keeping into account an increase in direct and indirect costs equal to what was registered in the financial statements of the South African holding. The extremely high profitability rates Aspen obtained from the investment in purchasing the Cosmos trademarks for the Italian market also prove the unreasonableness of the price levels imposed. Aspen's statement admits that it did not provide any relevant reason to justify the requested prices. To assess the fairness of Aspen's pricing through economic justification, a comparison was also made between the profits generated by each Cosmos drug and the investment made to acquire their trademarks, as well as the average return on capital in the generic drugs sector. The results show an internal rate of return (IRR) for each Cosmos product between 20-30% and 30-40%. Comparing the initial investment with the profit flows from excessive pricing, the percentages of returns on the capital invested vary from 10-20% to 30-40%. These percentages are compared to the average return on invested capital in the pharmaceutical industry, identified by various studies. The weighted average cost of capital (WACC) for the entire sector is approximately 8% and it is evident that the new prices charged by Aspen have revenues significantly superior to the WACC of the pharmaceutical sector.

- Potential qualitative factors related to the products: The investigation found no extra-economic benefits for patients or the SSN resulting from the price increases, as there were no qualitative improvements in the products or related services. Cosmos drugs were developed many years ago and have remained unchanged in their composition and formulation. No advantage for patients or the SSN followed the price increase, and Aspen's choices concerning the allocation of the product quantity in the price negotiation with AIFA worsened the issue of drug scarcity in Italy. The economic value of the service provided is correctly measured by the overall direct and indirect costs identified in the previous sections, without any consideration of other factors not reflected by costs that could increase the value. In addition, as previously motioned, for the case of life-saving products like oncologic pharmaceuticals lacking therapeutic substitutes, the concept of willingness to pay is inadmissible, and any price increase would be plausible, making exceedingly expensive prices unacceptable, regardless of the level of prices imposed. For this reason, the Party’s comparison with common consumption goods is not appropriate.
- The nature of the products under examination: The nature of the drugs under examination is a crucial factor in evaluating the unfairness of the prices imposed by Aspen. These drugs are

used to treat severe oncologic pathologies that affect sub-populations of vulnerable patients who have no therapeutic substitutes in certain phases of their disease. Due to their life-saving nature and lack of alternatives, doctors and patients strongly prefer therapeutic continuity with these products. This has created a high demand for Cosmos drugs, meaning that the National Health Service (SSN) and even patients who purchase the drugs are forced to bear the price increases imposed by Aspen due to its dominance in the market.

- The characteristics and business model of the Aspen group: Another significant factor in determining the unfairness of Aspen's pricing is the company's mission and purchasing strategy for the product portfolio under investigation in other European countries. Aspen is primarily a distributor of generic drugs and trademark drugs developed by other companies, with no significant research and development activities. For the products in question, which have had an expired patent for decades, Aspen does not invest in research and development or medical-scientific promotion, as confirmed by the company itself. This circumstance precludes the possibility of justifying the high prices as a means of recovering investments in product development. Aspen's purchasing of the anticancer package with an expired patent, but lacking replaceability, and the subsequent redefinition of price increases across various European countries, corresponds to a business model that exploits market niches to impose prices that are disproportionate to the costs borne or the service provided to consumers, and lacking any socially useful investments aimed at innovation. This aggressive pricing strategy does not appear to be an isolated occurrence.
- The rise in public healthcare expenses: According to data provided by AIFA, the total healthcare expenditure for the drugs in question increased from 1.5 million Euros in 2013 to approximately 6.4 million Euros in 2014, due to the price increases imposed by Aspen. These price increases had an impact for only eight months in the year, as the new prices were decided at the end of March 2014 and became effective from May 2014. As a result, the SSN and patients bore an expense for Aspen's drugs about five times higher than before the price increases, corresponding to a percentage increase in healthcare expenditure of about 500%. This has had a direct impact on the SSN's resources, which are limited and determined by the state budget. The dispersion of public funds caused by Aspen's abusive behavior in charging excessively high prices for these drugs has inevitably led to a reduction in funds available for other purposes falling within public healthcare policies.

After taking into consideration all these factors for the specific case, the price and cost difference was regarded as unreasonable, as there is no qualitative motivation that justifies the increase imposed by Aspen.

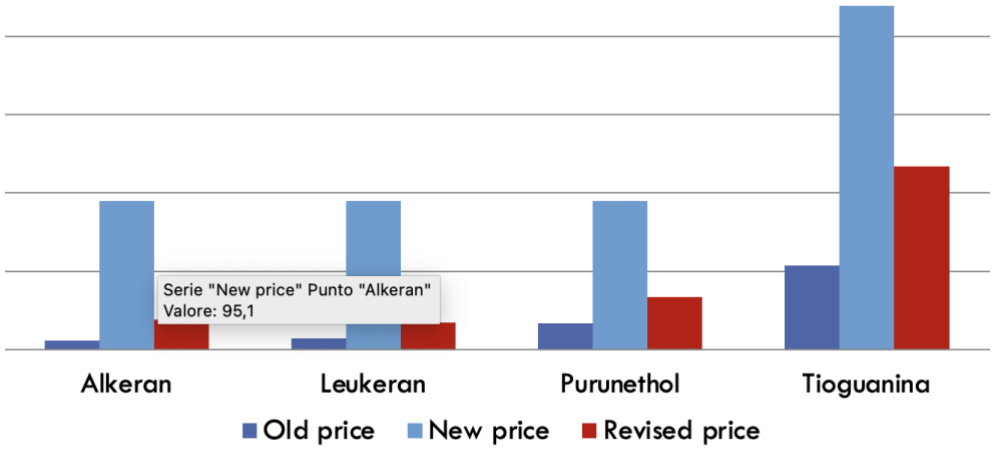
v. Case conclusion

In conclusion, the relevant markets of the products were defined at the ATC5 level, which corresponds to the single active ingredients of Aspen's drugs, and there is no therapeutic replaceability between Cosmos drugs and other specialty drugs available on the market for the same pathologies treated by Cosmos drugs. The absence of therapeutic replaceability was confirmed by scientific bodies and expert oncologists. The unique characteristics of Cosmos drugs, such as their formulation in tablets, high tolerability, and suitability for use in maintenance therapies at home, made them the only specialty drugs usable for certain forms of leukemia and weaker patients. The absence of relevant collateral effects characterizing Cosmos drugs was a key factor for considering their irreplaceability. Finally, there was no evidence that Aspen examined the competitive context of reference of Cosmos drugs during the price negotiation with AIFA. The Party's regression analysis, which infers that the volumes of Cosmos drugs decreased by 30-40% following the price increase, couldn't be considered as proof of replaceability with other drugs, as this reduction in consumption was more plausibly explained by a reduction in parallel exportations from Italy due to the alignment of Italian prices with the European average. Additionally, there was no evidence in the documentation collected during inspections or the proceedings that Aspen examined the competitive context to which the Cosmos drugs belonged. The only reference made in the documentation was to an international comparison of prices used to define the "floor price" of the negotiation with AIFA. Then the dominant position in the market of the undertaking was analyzed. The evaluation was based on the absence of actual and potential competition and the ability to behave independently from the regulator AIFA. In fact, even if there are no patent or legal barriers to producing generic versions, no direct competitive pressure was present at the time of negotiation with AIFA; Aspen is the only company with an AIC in Italy for drugs with the active ingredients used in Cosmos drugs. In addition, the markets have a contained economic dimension due to the low incidence of oncologic-hematological pathologies, and the demand for Cosmos drugs is rigid since it is characterized by a high preference for therapeutic continuity. Aspen's negotiation power and behavior of substantial independence with reference to AIFA were proven by the success of its negotiation strategy, and the absence of true power for the Italian Medicines Agency. Due to all these circumstances, Aspen held a stable dominant position in the relevant markets identified.

The company abused its dominant position through its aggressive negotiation strategy with AIFA by threatening to suspend the supply of essential oncological drugs for elderly and child patients if its proposals were not accepted. This strategy allowed Aspen to increase prices by 300% to 1500%, resulting in an extremely high price increase and an important surplus compared to the costs of the

drugs. As a matter of fact, the Cosmos drugs have been in commerce for several decades, and Aspen did not invest in research and promotion or make any qualitative improvements to the products. Finally, considering the forgoing, the investigation found that Aspen had violated Article 102 letter a) of the TFUE. The undertaking abused the dominant position it had on the relevant markets by imposing excessive and unfair prices for all the drugs previously cited. The AGCM fined Aspen 5 million euros, and the undertaking was required to stop its abusive conduct and inform the Authority within 60 days about the steps taken to comply with the decision. It was not specified by the Authority what prices the undertaking should set or how to set them. It was Aspen's responsibility to set prices that had a reasonable relationship with the economic value of the products and complied with EU and Italian competition laws. On June 13, 2018, the Italian Authority closed the proceedings against Aspen as it reached an agreement with AIFA. As the prices, relative to the ex-ante amount, were reduced to an increase in between 70% to 200%. Figure 9 shows the differences between the old prices, the new prices, and the revised prices for each Cosmos drug.

Figure 9 Revised Prices (en.agcm.it)



4. The Leadiant Case

4.1 Brief Introduction to the Leadiant Case

The Italian Competition and Market Authority has fined the pharmaceutical company Leadiant for charging an excessively high price for its drug Leadiant® Chenodesoxycholic Acid, taking advantage of its dominant market position. Given the vital importance of the drug, the Authority considered the infringement to be very serious and imposed a fine of about 3.5 million euros on Leadiant. This action started after a report by Altroconsumo to the Antitrust in 2019. According to the Antitrust, since 2017, Leadiant has imposed "unjustifiably burdensome prices for the sale of a life-saving drug"[16] on the Italian National Health Service. This drug is used to treat a rare disease that causes severe disability and leads to premature death in affected patients: the cerebrotendinous xanthomatosis (CTX). Leadiant® Chenodesoxycholic Acid is the only existing pharmacological treatment that, when taken daily, allows people with this condition to lead a normal life. Furthermore, Leadiant is the only company that produces and sells the drug in the European market, with no alternatives available.

According to the Antitrust, after a complex investigation, it emerged that the abuse committed was the result of a carefully planned strategy - conceived by the group many years before and pursued intentionally - and was also achieved through dilatory and obstructive behavior by Leadiant in the drug reimbursement price negotiation procedure with AIFA. Chenodeoxycholic acid is not an innovative active ingredient, but it is a very old drug that has been on the market since the 1970s and was sold by several companies in Europe about 15/20 years ago, until these firms stopped selling it due to lack of commercial interest. Chenodeoxycholic acid was used for the treatment of gallstones but was gradually abandoned for treatments with other more effective and safer medications. In addition to the "official" treatment for gallstones, the CDCA-based drug was also informally used for cerebrotendinous xanthomatosis. The pharmacological treatment based on chenodeoxycholic acid quickly proved to be the only safe and effective treatment for patients with this rare disease, allowing them to live a normal life. It was also a very inexpensive treatment: in Italy in the 1990s, a capsule costed about 30 and 35 euro cents. Thus, it was an essential and very low-cost treatment, although not formally authorized, it is the so-called off-label use, that is, outside the formal indication, which remained that of gallstone treatment. However, all this changed when various manufacturers stopped marketing CDCA in the 1990s or sold their production branches to Leadiant, which effectively

[16] www.altroconsumo.it. (n.d.). *Farmaci troppo cari: a Leadiant una sanzione di circa 3,5 milioni di euro per abuso di posizione dominante | Altroconsumo*. [online] Available at: https://www.altroconsumo.it/salute/farmaci/news/farmaci-cari-sanzione-antitrust.

became the only pharmaceutical company selling this drug in the European market by the end of the first decade of the 2000s. From that moment on, there were gradual and substantial price increases, reaching 15,500 euros package in 2017, after being formally authorized by EMA (European Medicines Agency) for the treatment of cerebrotendinous xanthomatosis. Although the drug was not patent protected, the company could still benefit from a ten-year monopoly. The authorization to market an orphan drug, a medicine used to treat a rare disease, comes with the granting of protection from competition in the European market for ten years. This reward is provided by law to compensate companies investing in rare diseases and to encourage innovation in an area that had little commercial interest until a few years ago. Unable to forego purchasing the drug, health services and hospitals in several European countries, including the Netherlands and Italy, initially tried to buy the medicine at more affordable prices from foreign markets or, if unable to find low-cost formulations, resorted to galenic formulations prepared by hospital pharmacies that treated the patients. In this latter case, it was still possible to guarantee high-quality production at lower prices than those requested by Leadiant. But this possibility also ran out over time: increasingly, foreign formulations were no longer available, and hospitals eventually no longer had access to the raw material. All that remained was to purchase Leadiant's drug at the requested price. The pharmaceutical company thus managed to transform an old, inexpensive, and non-patented drug into a multi-million euro investment.

The Italian fine comes after the Dutch one. In fact, Leadiant had already been fined in the Netherlands in 2021 with a fine of about 20 million euros. According to the Dutch competition and market regulator, Leadiant exploited its position of strength to impose an excessively high and unjustified price. In fact, the cost of the drug was not commensurate with the modest investments the company made to bring the drug to market, and this allowed the drug company to make huge profits from the treatment of a rare disease, despite the low risks and costs incurred. As the Chenodesoxycholic acid (CDCA) was not a new or innovative drug and Leadiant did not invent it. Instead, it is a long-standing drug, marketed in Europe for decades to treat the disease in question long before the pharmaceutical company began selling it at a price hundreds of times higher than it was until 30 years ago, when it was manufactured by multiple companies. Therefore, the price was unfair, or rather, unjustified, since the drug had already been in use for some time, under a different name and at a much lower cost. Leadiant did not introduce any innovations to the market and, consequently, did not make any investments to justify such a high price. The regulator believed that one-third of the price would have been more than enough to generate significant profits. However, Leadiant took advantage of its dominant position in the market, being the only company to produce the drug, to negotiate with the Dutch Ministry of Health and insurance companies for an excessive price. As a result, the authority decided to impose a fine of approximately 20 million. In Italy, the initial price was about 15,500 euros

per pack, which was reduced only in December 2019 after the Authority launched its investigation and yet, according to economic analyses conducted, still too onerous and unfair, and it fined the company 3,5 million euros.

4.2 Leadiant's Case Analysis

i. Premise

The investigation conducted by the AGCM[17] was first of all made to ascertain that in the Italian market for CDCA-based drugs used to treat a rare disease, the CTX, Leadiant possessed a dominant position, a monopoly, acquired since the beginning of 2016. Furthermore, how the elements acquired by the Authority indicated that Leadiant, since June 2017, had abused its market position through a negotiating conduct adopted towards the AIFA which allowed it to impose unjustifiably burdensome prices on the Italian SSN for the sale of CDCA Leadiant®. This abuse results from a very articulated strategy, conceived a long time ago and intentionally cultivated for several years by the dominant company, aiming to create the appropriate context to allow the effective application of its abusive pricing policy.

In 2008, Leadiant acquired a drug based on CDCA, which was certified for the cure of gallstones but had been used, almost entirely, off-label for the treatment of CTX. This acquisition made the dominant company the only operator in Europe to market this drug. Leadiant's ultimate goal was to obtain orphan drug designation and register it for the treatment of CTX. Leadiant took a significant stride in accomplishing its objective by securing a supply agreement that granted them sole possession of the active component of the drug. This was made possible by partnering with the only reputable CDCA supplier in Europe, PCA - an Italian chemical company. Leadiant launched CDCA Leadiant® in the local market in June 2017 and initiated talks with AIFA to establish the orphan drug's price. The company proposed a package price of €15,506.97. However, AIFA deemed this price unjustified, as the company did not provide a detailed breakdown of costs or consider the value of the drug's therapeutic benefits. Despite this, the dominant company adopted a delaying and antithetical approach, prolonging the procedure for around two and a half years. This put AIFA in a weak position, as the National Health Service needed to provide patients with an indispensable, irreplaceable, life-

[17] www.agcm.it. (n.d.). *AGCM - Autorita' Garante della Concorrenza e del Mercato*. [online] Available at: https://www.agcm.it/dettaglio?db=41256297003874BD&uid=5F6041FF7929D043C125849B0046F058&view=&title=A524-LEADIANT%20BIOSCENCES/FARMACO%20PER%20LA%20CURA%20DELLA%20XANTOMATOSI%20CEREBROTENDINEA&fs=Abuso%20di%20posizione%20dominante [Accessed 21 May 2023].

saving drug at an acceptable cost within a reasonable timeframe. Exploiting this fragility, the dominant company was able to attain a price, ex-factory, for the orphan drug between € 5,000 and € 7,000 per package, which, despite being significantly lower than the price proposed at the beginning, was still unfounded burdensome. The price was disproportionate to the overall costs incurred and unfair given the nature of the product, research and development investments, risk taken in the registration project, and the therapeutic value attributed to CDCA Leadiant® by AIFA and medical professionals. It is believed that the negotiated price would have been even higher without the Authority's intervention, and thus more out of proportion and even less justified according to the parameters. This conduct made the National Health Service incur significantly higher expenses to purchase the drug. In summary, for the reasons that will be better and more thoroughly argued in the following sections, it is considered that Leadiant has put in place, starting from June 15, 2017, an illegitimate conduct according to Article 102, lett. a), of the TFEU, since it has abusively exploited its dominant position to charge unjustifiably burdensome prices for the sale of the orphan drug called CDCA Leadiant® to the SSN.

ii. Leadiant strategy

At a time when there was no longer any interest in Europe in selling medicines based on CDCA for the treatment of gallstones, as the active ingredient had been supplanted by other treatments, and companies were gradually exiting the market, the only valid economic reason to enter was to gain access to another niche market, which was extremely small but potentially very profitable due to the significantly high prices generally granted to orphan drugs: that of CTX, which had been treated with CDCA for decades. This was, in fact, Sigma Tau's aim. However, in order to achieve this objective, Sigma Tau had to assure that there were no other companies in the European market that marketed CDCA-based drugs, and, in this way, that the company would become a monopolist in the CDCA drug market in Europe. Therefore, in 2008, the company considered acquiring the four AICs related to the few CDCA-based drugs registered for the treatment of gallstones still present in the EU, such as Quenobilan® and Quenocol® in Spain, Xebyl® in Portugal, and the Chenofalk® valid for the Netherlands, in order to eliminate them from the market. However, when Sigma Tau made these evaluations, the structure of national markets for CDCA-based drugs had naturally undergone further changes that made such acquisitions unnecessary and facilitated Sigma Tau in achieving its goal. The aforementioned, Spanish products had in fact been withdrawn from the market, with the consequent revocation of their AIC, between the end of 2008 and the beginning of 2009. Therefore, only the "competing" AIC of Chenofalk® valid for the Netherlands remained, which Sigma Tau purchased in September 2009 and strategically kept valid without ever using it, until it expressly renounced it on

September 9, 2015. Similarly, the AIC of Xebyl® remained inactive after the drug was not marketed from the beginning of 2011.

In essence, therefore, the documentation on record clearly indicates that from the beginning of 2011, there was only one CDCA-based drug available on the market in Europe, Xenbilox®, owned by Sigma Tau. Once Xenbilox® became an essential off-label cure for CTX, the holding increased the price of the drug, before obtaining the AIC for Leadiant® CDCA as a means of preparing the market for the future price of the on-label orphan drug, the so-called "step price increase". Furthermore, the company created an artificial differentiation between Xenbilox® and Leadiant® CDCA, called "brand differentiation", achieved through the withdrawal of the former drug from the market upon the introduction of the latter and the attribution of orphan drug status to a company different from the one that held the off-label drug's ownership. This approach enabled the dominant company to demonstrate to the relevant authorities that Leadiant GmbH had no connections with Sigma Tau Arzneimittel GmbH and that the orphan drug was not in any way associated with Xenbilox®, thus supporting their case, allowing the company to charge a higher price for the Leadiant® CDCA drug.

For what concerns the company's negotiations with AIFA, based on the available evidence, it appears that during the negotiation process for the reimbursement price of the orphan drug, Leadiant intentionally adopted a delaying and obstructive attitude towards AIFA. In fact, for a year and a half, despite repeated requests from the Agency, the dominant company did not provide any information or documentation on research and development investments that could adequately support their initial price proposal of 15,506.93 euros per package, or subsequent ones, and justify the price difference between Leadiant® CDCA and Xenbilox®. Additionally, Leadiant strategically prolonged the negotiation process by submitting corrective economic offers late in comparison to the initial one.

iii. The relevant market

As previously discussed, in the pharmaceutical sector, the identification of the relevant market for a product is based on the concept of therapeutic substitutability of medicines, which is determined primarily by the ATC classification system. However, additional factors such as prescribing trends, institutional demand and supply organization, and a drug's efficacy in treating a specific condition may warrant a more specific analysis of substitutability. Regarding the geographic market, the prevailing practice is to consider the competitive scope as national due to institutional differences in healthcare systems and pharmaceutical policies, as well as varying epidemiological conditions and

financial resources among member states. However, there is a growing trend towards harmonization at the EU level, particularly in access-to-market regulations.

The market affected by this measure is the market for the production and sale of medicines for the treatment of an ultra-rare disease, CTX. Typically, the demand for drugs used to treat CTX is expressed by specialist doctors who care for patients in hospitals where they operate, and therefore by the Local Health Authorities (ASL) who purchase these drugs at the request of those doctors, which are then commercialized through the hospital channel. According to the investigation, various therapies have been used by doctors to treat this disease, such as CDCA-based drugs, and in limited cases, medicines based on cholic acid, ursodeoxycholic acid, and statins (particularly, simvastatin, lovastatin, and pravastatin), in combination with CDCA. Chenodeoxycholic acid Leadiant is among the drugs used to treat bile disorders with ATC3 code. Other active ingredients used off-label for the treatment of CTX include cholic acid, with ATC5 code, and ursodeoxycholic acid with ATC5 code, which are also part of the therapeutic subgroup of bile acids and their derivatives. Simvastatin, lovastatin, and pravastatin all belonged to the ATC5 code under the therapeutic class of HMG-CoA reductase inhibitors (ATC4 code).

According to the investigation, CDCA-based drugs, other than the orphan drug marketed by Leadiant, have not been available on the Italian market for some time. As previously mentioned, due to the obsolescence of chenodeoxycholic acid in the treatment of gallstones and the small size of the market for the treatment of CTX since the mid-1990s, companies that marketed such drugs have left the domestic market. Galenic preparations based on CDCA were available in the Italian market from 1997 to 2016 to address the shortage of industrially produced drugs containing this active ingredient and to ensure therapeutic continuity for patients with CTX. However, galenic preparations ceased in November 2015 due to a lack of raw materials in the Italian market. From that moment until the introduction of the CDCA Leadiant® orphan drug for the treatment of the rare disease CTX in Italy, Xenbilox® was used off-label as the only CDCA-based drug available in Europe at that time and owned by the company. In June 2017, the Chenodeoxycholic Acid Leadiant® was introduced in the domestic market and from that moment has been the only CDCA-based product available for the treatment of CTX.

During the proceedings, it was also found that Kolbam®, a drug based on cholic acid, which was a possible substitute, has never been authorized in Italy, and that, in any case, the marketing authorization granted by the European Commission was revoked in July 2020. Therefore, it cannot

be imported from abroad. The other cholic acid-based drug, Orphacol®, has been authorized for the treatment of congenital defects in the synthesis of primary bile acids other than those that cause CTX and as such is also marketed in Italy. In addition, there are no ursodeoxycholic acid or statin-based drugs marketed in Italy and used for the treatment of CTX.

In conclusion, the documentation acquired during the investigation clearly indicates that there is no therapeutic interchangeability between the above-mentioned drugs. This emerges both from the trend of prescribing choices made by doctors over a time period that extends at least from 2014 to the present day, and from the evaluations expressed by the doctors themselves on the efficacy of the drugs in treating CTX. From the point of view of the prescribing pattern adopted by doctors, CDCA has always been the therapy of choice for CTX in all European Union Member States where the disease is present. The efficacy of CDCA in the treatment of the rare disease is, in fact, recognized, at the scientific level, the empirical level, in clinical practice, and at the institutional level. In this regard, one of the world's leading experts on CTX confirmed that CDCA should be "preferred in the treatment of the rare disease under consideration" and that "there is a clear consensus in the international medical-scientific community that CDCA is the therapy of choice for CTX". The evidence collected during the investigation indicates that this is particularly true for Italy, where the active ingredient has been used for about forty years, in a substantial exclusive way, in the treatment of the rare disease. Moreover, several pieces of evidence gathered during the investigation show that in terms of efficacy in treating CTX, CDCA is considered superior to cholic acid, which in turn is considered superior to ursodeoxycholic acid. Cholic acid is used only rarely, in the rare cases where CDCA causes side effects. In particular, doctors, especially Italian ones, do not prescribe cholic acid for the treatment of the rare disease, nor do they replace CDCA with cholic acid in non-naïve patients, as the active ingredient, while lowering bile acid levels, does not appreciably affect the clinical picture of patients. This is confirmed by the absence of evidence indicating that Orphacol®, although available on the market, including the domestic one, before Chenodeoxycholic Acid Leadiant® was ever prescribed, off-label, for the treatment of the rare disease under consideration. The preference of doctors for CDCA over cholic acid was even maintained during the period of about three years in which Kolbam® was the only authorized drug for CTX. In other words, they preferred to prescribe an off-label drug instead of an on-label drug precisely because of the therapeutic superiority of the former, even though this was not formally recognized on a regulatory level. The non-therapeutic equivalence between CDCA and cholic acid has also been affirmed by EMA itself, based on the evidence produced by the same pharmaceutical company to demonstrate the existence of "significant beneficial effects" of CDCA over cholic acid. Therefore, given the minimal therapeutic substitutability of

CDCA with cholic acid for the treatment of CTX, it is believed that the latter molecule is not able to exert a competitive constraint on the former sufficient to consider both as belonging to the same relevant market. Consequently, Orphacol® cannot be considered an effective and actual competitor of Chenodeoxycholic Acid Leadiant® and, therefore, cannot be included in the same relevant market. Similar considerations can be made for ursodeoxycholic acid and statins, for which there is very limited clinical practice, which, in any case, reveals, especially according to Italian doctors, the absence of an appreciable effect in correcting metabolic alterations present in CTX.

Therefore, in light of the consolidated jurisprudential principles on the definition of the relevant market in the pharmaceutical sector, reiterated in the ruling of the Council of State on the Aspen case, it is correct in this case to circumscribe the relevant market at the level of the single active ingredient ,at a ATC5 level, and to define it, from a product point of view, as inclusive only of CDCA-based drugs, ATC5 code. Furthermore, for the already mentioned reasons related to the specificities of the SSN, the level of epidemiological diffusion of the disease in the Italian territory, and the different willingness to pay of Italy compared to other Member States, it is believed that even in this case, the market for the above-identified product is limited to the national territory.

iv. Leadiant's dominant position

There are different reasons why Leadiant was found to hold a dominant position in the relevant market. Foremost, Leadiant is the only company operating in the market since the beginning of 2016. The exclusive supply agreement for CDCA signed in 2008 between Sigma Tau, the group's holding, and PCA, the only credible producer of this resource in Europe, gave Leadiant control of the raw material, creating a contractual barrier for CDCA and, in particular, for producers of galenic drugs based on the same molecule. This closed, starting from January 2016, the domestic market of magistral preparations[18] - medicinal products prepared in a pharmacy for an individual patient in accordance with a prescription from a doctor - allowing the company to become the only operator on the Italian market with the sale of Xenbilox®. Moreover, starting from April 2017, Leadiant benefited from a double regulatory barrier, valid both against competing manufacturers of CDCA-based industrial drugs used to treat CTX and against competing manufacturers of magistral preparations based on the same molecule. The acquisition of the orphan drug designation, AIC, enabled Leadiant to obtain a ten-year market exclusivity preventing the registration of other similar products to CDCA Leadiant® for the treatment of the rare disease, CTX. Additionally, the Italian law prohibited the

[18] Magistral medicines https://laegemiddelstyrelsen.dk/en/pharmacies/pharmacies/magistral-medicines/

production of magistral drugs when there was an industrial product registered for a specific therapeutic indication. In this way, since June 2017, patients with CTX in Italy have been treated only with Leadiant's orphan drug. On top of that, Leadiant deliberately downplayed the highly significant factor of the extremely small size of the market, which would have discouraged new entrants, in the unlikely scenario that they were able to find another source of CDCA production. This is confirmed by Leadiant's own statements, which can be found in the inspection documentation, where the company considered the entry of new drugs into the market highly unlikely due to its small size. It should be noted that the cited document dates back to September 2014, which is after the price increase of Xenbilox® to 2,900 euros per package that occurred in July 2014, making the drug highly profitable for Sigma Tau. Several elements in the record suggest that this situation will continue in the coming years, at least until the expiration of Leadiant's patent, in April 2027. Leadiant disputed this reconstruction, claiming that the exclusive agreements between Sigma Tau and PCA did not close the market to magistral preparations and that the sales of Xenbilox® in Italy between 2016 and 2017 were managed by a third party. Furthermore, the company claimed that its ability to exercise market power has been and will continue to be limited by competitive dynamics in other EU member states. However, the investigation has shown that, in early 2016, Leadiant extended its dominant position in Italy, thanks to the sale of the only CDCA-based drug then available, Xenbilox®, and consolidated this market position through the acquisition of the orphan drug designation also for the Italian territory. In fact, the company extended the dominant position, that it already had in the other national markets of the European Union, in Italy thanks to the Xenbilox® drug.

v. Price Analysis in Italy: excessiveness and unfairness

An enterprise in a dominating position is prohibited under Article 102(a) TFEU from enforcing unfair purchase or selling prices or other unfair trading conditions directly or indirectly. This includes prohibiting the imposition of unreasonably onerous pricing that are not supported by any justifiable cause. As previously said, in the United Brands decision, the Court of Justice of the European Union ruled that a price is illegal under this provision when an undertaking has derived commercial advantages through the use of its dominant position that it would not have obtained had there been regular and sufficiently effective competition in the relevant market. Due to this, it appears that the price charged does not reasonably reflect the economic value of the service provided. It is widely accepted that there is no one approach to assessing the relationship between a good or service's economic value and its price. Instead, the Court itself has noted that many techniques can be employed to establish whether a price set by a dominating undertaking is excessive, unfair, and hence abusive. One of these techniques relies on a "comparison between the selling price of the in-question product

and its cost of manufacture [...] from which would arise the amount of the profit margin. According to the approach outlined by the European courts, this price-cost comparison examination is conducted in two stages: The purpose of the first is to determine "whether there is an excessive disproportion between the cost actually incurred and the price actually charged," while the purpose of the second is to determine whether the excessive price in relation to costs is also "not fair, either in absolute terms or in relation to competing products." It should be mentioned that when it comes to commodities on which consumers are entirely dependent, as in the current situation, the examination to uncover potential grounds for the disparity between prices and costs must be more stringent. Having said that, the application of these principles to the current situation demonstrates that Leadiant used its dominant position to charge excessively high prices that had nothing to do with the economic value of the service being provided and were solely set up to gain a competitive advantage. In other words, the dominant company's prices for the orphan drug's sale in Italy are excessive and unreasonable, and as a result, they breach Article 102(a) TFEU.

A. Excessive prices

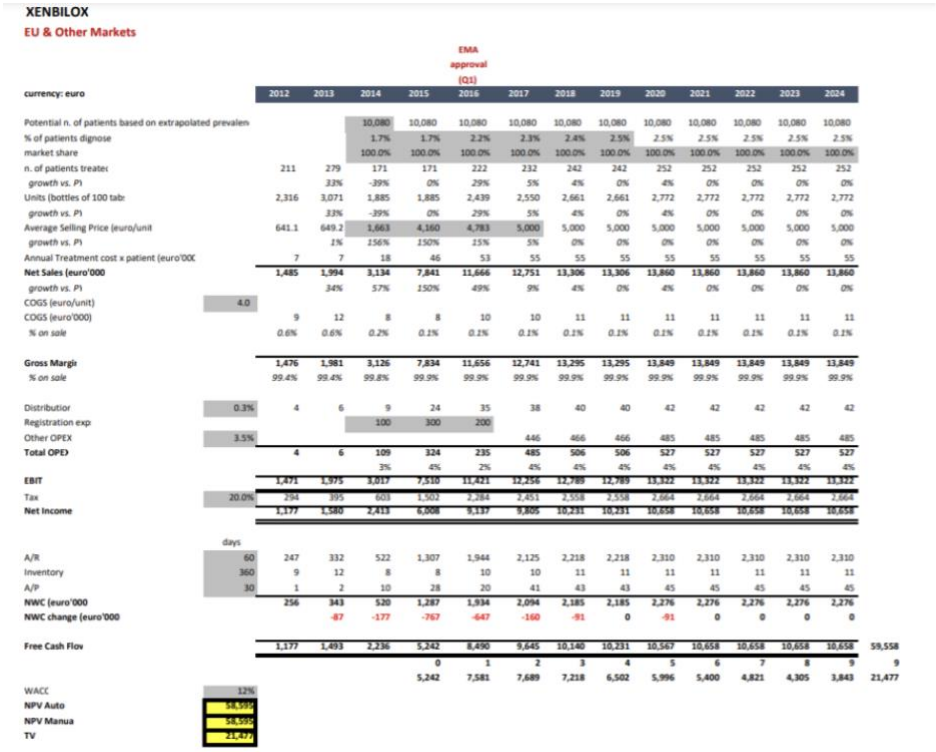
Regarding the determination of the economic value of the service provided, which is necessary for the first part of the United Brands test, it is believed, based on established practice and case law, that this value should reflect, at a minimum, the costs incurred by the dominant enterprise in producing the good or service. Preliminary analysis reveals that the Leadiant® CDCA's price level was never based on the costs incurred by the dominant firm, as evidenced by numerous documents in the record. Instead, Leadiant's various price assumptions were based on their expectations of the highest price that demand would be willing to pay for the drug, regardless of any costs incurred. In particular, the quantification of the total costs associated with the registration of CDCA Leadiant® that the dominant company had internally conducted to support the requested price reveal, in fact, a level of costs far removed from that which would have justified such a high price, so much so that this figure was not provided in the negotiation with the Regulatory Authority. A different and more extensive reconstruction of the costs was elaborated only *a posteriori*, in the study commissioned from the consulting firm Copenhagen Economics as part of the antitrust proceedings initiated by the Dutch Competition Authority under Article 102(a) TFEU. Although not mandatorily required by the EU Court of Justice's jurisprudence, two different methodologies were used to assess the excessiveness of the price. One was of a financial nature, and the other was of an accounting nature, which allowed for a robustness check of the analysis carried out. This approach aligns with that part of legal and economic doctrine that encourages the parallel application of several methodologies. The investigative activity has shown a significant disproportion between the prices charged in Italy for

the sale of CDCA Leadiant® to the SSN and the value of this drug, which must reflect the costs for its production, marketing, and maintenance on the Italian market.

Financial methodology

The first methodology utilized by the AGCM considers the internal rate of return (IRR) of the CDCA project, which was initiated in 2014 with the increase in the price of Xenbilox® and the request for orphan designation for CDCA with the new therapeutic indication and will conclude in 2027 at the expiration of Leadiant's market exclusivity for CDCA. The goal of investment project analysis, also known as capital budgeting analysis, in corporate finance is to determine which projects should be taken on in order to maximize shareholder value. To do this, this methodology is used to calculate the project's anticipated internal rate of return and compare it to the cost of capital the company will sustain to implement the project. The project is profitable, and the firm is consequently motivated to start it if the estimated rate of return is greater than the cost of capital. Otherwise, the business won't be motivated to start the project. The IRR analysis is, indeed, typically done by a company ex-ante in order to understand whether to initiate a project or not, in fact, Sigma Tau itself used it to understand the profitability of the CDCA project. The economic analysis done by the undertaking showed a great incentive to ask for a designation for CDCA and an AIC in Europe for the treatment of the new therapeutic indication, in fact the calculated profitability according top Sigma Tau had a gross contribution margin of 99%. In particular, the undertaking identified ex-ante, two scenarios for the role of Xenbilox® in Europe, assuming the marketing of the orphan drug starting in 2016: a baseline, more cautious scenario assumed a modest increase- from 1.7 percent to 2.5 percent- in the rate of disease diagnosis among the affected population in the absence of changes to the company's operating model. A more optimistic scenario assumed that, in the face of increased costs incurred by the company to improve the diagnosis of the disease, the illness would come to be diagnosed in 10% of cases. The first case is called the “base case” scenario and the latter “best case” scenario. Figure 10 and 11 respectively show the results of each scenario. To assess the project's profitability, the two IRR values were compared with the project's cost of capital (WACC) as quantified by Leadiant itself in the project's start-up phases, as an ex-ante valuation: 12% in the base case and 15% in the best case, the latter identified as riskier.

Figure 10 Best case scenario (en.agcm.it)

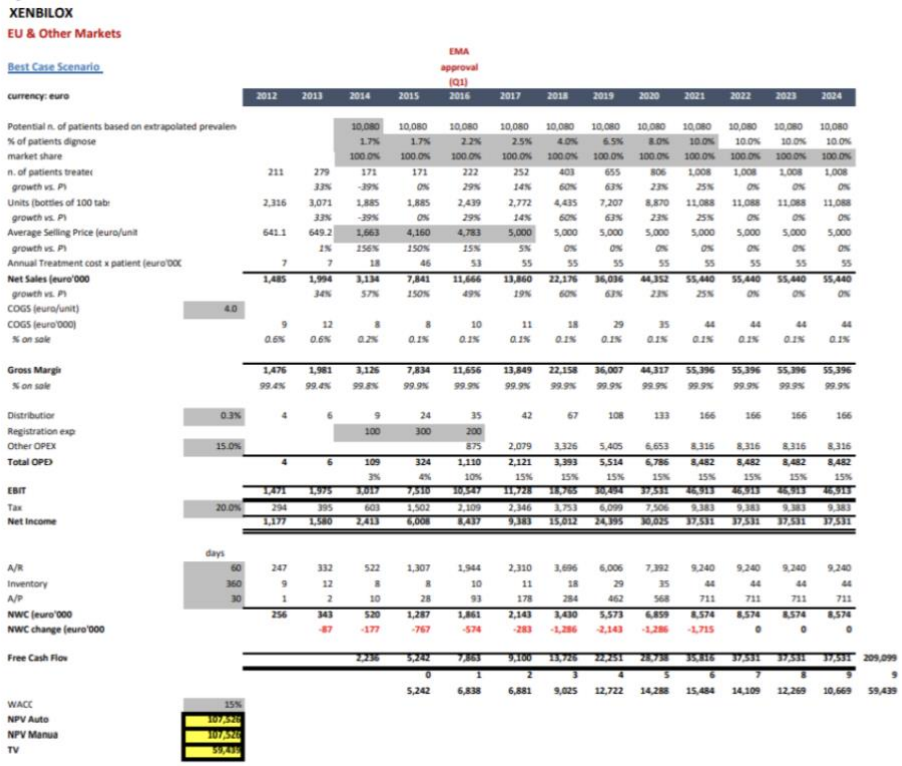


XENBILOX

EU & Other Markets

currency: euro		2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	
						EMA approval (Q1)									
Potential n. of patients based on extrapolated prevalen				10,080	10,080	10,080	10,080	10,080	10,080	10,080	10,080	10,080	10,080	10,080	
% of patients dignose				1.7%	1.7%	2.2%	2.3%	2.4%	2.5%	2.5%	2.5%	2.5%	2.5%	2.5%	
market share				100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	
n. of patients treate		211	279	171	171	222	232	242	242	252	252	252	252	252	
growth vs. PY			*33%*	*-39%*	*0%*	*29%*	*5%*	*4%*	*0%*	*4%*	*0%*	*0%*	*0%*	*0%*	
Units (bottles of 100 tab		2,316	3,071	1,885	1,885	2,439	2,550	2,661	2,661	2,772	2,772	2,772	2,772	2,772	
growth vs. PY			*33%*	*-39%*	*0%*	*29%*	*5%*	*4%*	*0%*	*4%*	*0%*	*0%*	*0%*	*0%*	
Average Selling Price (euro/unit		641.1	649.2	1,663	4,160	4,783	5,000	5,000	5,000	5,000	5,000	5,000	5,000	5,000	
growth vs. PY			*1%*	*156%*	*150%*	*15%*	*5%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	
Annual Treatment cost x patient (euro'00(		7	7	18	46	53	55	55	55	55	55	55	55	55	
Net Sales (euro'000		**1,485**	**1,994**	**3,134**	**7,841**	**11,666**	**12,751**	**13,306**	**13,306**	**13,860**	**13,860**	**13,860**	**13,860**	**13,860**	
growth vs. PY			*34%*	*57%*	*150%*	*49%*	*9%*	*4%*	*0%*	*4%*	*0%*	*0%*	*0%*	*0%*	
COGS (euro/unit)	4.0														
COGS (euro'000)		9	12	8	8	10	10	11	11	11	11	11	11	11	
% on sale		*0.6%*	*0.6%*	*0.2%*	*0.1%*	*0.1%*	*0.1%*	*0.1%*	*0.1%*	*0.1%*	*0.1%*	*0.1%*	*0.1%*	*0.1%*	
Gross Margi		**1,476**	**1,981**	**3,126**	**7,834**	**11,656**	**12,741**	**13,295**	**13,295**	**13,849**	**13,849**	**13,849**	**13,849**	**13,849**	
% on sale		*99.4%*	*99.4%*	*99.8%*	*99.9%*	*99.9%*	*99.9%*	*99.9%*	*99.9%*	*99.9%*	*99.9%*	*99.9%*	*99.9%*	*99.9%*	
Distributior	0.3%	4	6	9	24	35	38	40	40	42	42	42	42	42	
Registration exp				100	300	200									
Other OPEX	3.5%						446	466	466	485	485	485	485	485	
Total OPE		**4**	**6**	**109**	**324**	**235**	**485**	**506**	**506**	**527**	**527**	**527**	**527**	**527**	
				3%	4%	2%	4%	4%	4%	4%	4%	4%	4%	4%	
EBIT		**1,471**	**1,975**	**3,017**	**7,510**	**11,421**	**12,256**	**12,789**	**12,789**	**13,322**	**13,322**	**13,322**	**13,322**	**13,322**	
Tax	20.0%	294	395	603	1,502	2,284	2,451	2,558	2,558	2,664	2,664	2,664	2,664	2,664	
Net Income		**1,177**	**1,580**	**2,413**	**6,008**	**9,137**	**9,805**	**10,231**	**10,231**	**10,658**	**10,658**	**10,658**	**10,658**	**10,658**	
	days														
A/R	60	247	332	522	1,307	1,944	2,125	2,218	2,218	2,310	2,310	2,310	2,310	2,310	
Inventory	360	9	12	8	8	10	10	11	11	11	11	11	11	11	
A/P	30	1	2	10	28	20	41	43	43	45	45	45	45	45	
NWC (euro'000		**256**	**343**	**520**	**1,287**	**1,934**	**2,094**	**2,185**	**2,185**	**2,276**	**2,276**	**2,276**	**2,276**	**2,276**	
NWC change (euro'000			**-87**	**-177**	**-767**	**-647**	**-160**	**-91**	**0**	**-91**	**0**	**0**	**0**	**0**	
Free Cash Flov		**1,177**	**1,493**	**2,236**	**5,242**	**8,490**	**9,645**	**10,140**	**10,231**	**10,567**	**10,658**	**10,658**	**10,658**	**10,658**	**59,558**
						0	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9** **9**
						5,242	**7,581**	**7,689**	**7,218**	**6,502**	**5,996**	**5,400**	**4,821**	**4,305**	**3,843** **21,477**
WACC	12%														
NPV Auto	58,999														
NPV Manua	58,999														
TV	21,477														

Figure 11 Best case scenario (en.agcm.it)



XENBILOX

EU & Other Markets

Best Case Scenario

currency: euro		2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	
						EMA approval (Q1)									
Potential n. of patients based on extrapolated prevalen				10,080	10,080	10,080	10,080	10,080	10,080	10,080	10,080	10,080	10,080	10,080	
% of patients dignose				1.7%	1.7%	2.2%	2.5%	4.0%	6.5%	8.0%	10.0%	10.0%	10.0%	10.0%	
market share				100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	
n. of patients treate		211	279	171	171	222	252	403	655	806	1,008	1,008	1,008	1,008	
growth vs. PY			*33%*	*-39%*	*0%*	*29%*	*14%*	*60%*	*63%*	*23%*	*25%*	*0%*	*0%*	*0%*	
Units (bottles of 100 tab		2,316	3,071	1,885	1,885	2,439	2,772	4,435	7,207	8,870	11,088	11,088	11,088	11,088	
growth vs. PY			*33%*	*-39%*	*0%*	*29%*	*14%*	*60%*	*63%*	*23%*	*25%*	*0%*	*0%*	*0%*	
Average Selling Price (euro/unit		641.1	649.2	1,663	4,160	4,783	5,000	5,000	5,000	5,000	5,000	5,000	5,000	5,000	
growth vs. PY			*1%*	*156%*	*150%*	*15%*	*5%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	
Annual Treatment cost x patient (euro'00(		7	7	18	46	53	55	55	55	55	55	55	55	55	
Net Sales (euro'000		**1,485**	**1,994**	**3,134**	**7,841**	**11,666**	**13,860**	**22,176**	**36,036**	**44,352**	**55,440**	**55,440**	**55,440**	**55,440**	
growth vs. PY			*34%*	*57%*	*150%*	*49%*	*19%*	*60%*	*63%*	*23%*	*25%*	*0%*	*0%*	*0%*	
COGS (euro/unit)	4.0														
COGS (euro'000)		9	12	8	8	10	11	18	29	35	44	44	44	44	
% on sale		*0.6%*	*0.6%*	*0.2%*	*0.1%*	*0.1%*	*0.1%*	*0.1%*	*0.1%*	*0.1%*	*0.1%*	*0.1%*	*0.1%*	*0.1%*	
Gross Margi		**1,476**	**1,981**	**3,126**	**7,834**	**11,656**	**13,849**	**22,158**	**36,007**	**44,317**	**55,396**	**55,396**	**55,396**	**55,396**	
% on sale		*99.4%*	*99.4%*	*99.8%*	*99.9%*	*99.9%*	*99.9%*	*99.9%*	*99.9%*	*99.9%*	*99.9%*	*99.9%*	*99.9%*	*99.9%*	
Distributior	0.3%	4	6	9	24	35	42	67	108	133	166	166	166	166	
Registration exp				100	300	200									
Other OPEX	15.0%					875	2,079	3,326	5,405	6,653	8,316	8,316	8,316	8,316	
Total OPE		**4**	**6**	**109**	**324**	**1,110**	**2,121**	**3,393**	**5,514**	**6,786**	**8,482**	**8,482**	**8,482**	**8,482**	
				3%	4%	10%	15%	15%	15%	15%	15%	15%	15%	15%	
EBIT		**1,471**	**1,975**	**3,017**	**7,510**	**10,547**	**11,728**	**18,765**	**30,494**	**37,531**	**46,913**	**46,913**	**46,913**	**46,913**	
Tax	20.0%	294	395	603	1,502	2,109	2,346	3,753	6,099	7,506	9,383	9,383	9,383	9,383	
Net Income		**1,177**	**1,580**	**2,413**	**6,008**	**8,437**	**9,383**	**15,012**	**24,395**	**30,025**	**37,531**	**37,531**	**37,531**	**37,531**	
	days														
A/R	60	247	332	522	1,307	1,944	2,310	3,696	6,006	7,392	9,240	9,240	9,240	9,240	
Inventory	360	9	12	8	8	10	11	18	29	35	44	44	44	44	
A/P	30	1	2	10	28	93	178	284	462	568	711	711	711	711	
NWC (euro'000		**256**	**343**	**520**	**1,287**	**1,861**	**2,143**	**3,430**	**5,573**	**6,859**	**8,574**	**8,574**	**8,574**	**8,574**	
NWC change (euro'000			**-87**	**-177**	**-767**	**-574**	**-283**	**-1,286**	**-2,143**	**-1,286**	**-1,715**	**0**	**0**	**0**	
Free Cash Flov				**2,236**	**5,242**	**7,863**	**9,100**	**13,726**	**22,251**	**28,738**	**35,816**	**37,531**	**37,531**	**37,531**	**209,099**
						0	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9** **9**
						5,242	**6,838**	**6,881**	**9,025**	**12,722**	**14,288**	**15,484**	**14,109**	**12,269**	**10,669** **59,439**
WACC	15%														
NPV Auto	107,526														
NPV Manua	107,526														
TV	59,439														

Sigma Tau estimated an NPV of more than €58 million in the "base case" scenario by discounting the anticipated cash flows over the period between 2015 and 2024 using a project WACC of 12%. In the "best case" scenario, the NPV exceeded €107 million while discounting the anticipated cash flows through a project WACC of 15%, higher than in the first scenario, to account for the added risk caused by the higher costs necessary to improve the diagnosis of the disease, and thereby increase sales volumes. Since Sigma Tau anticipated generating positive cash flows every year in either of the two scenarios, the IRR calculated using these data turns out to have infinite value. These findings are the result of the fact that Sigma Tau had already planned to raise the ex-factory price of Xenbilox® from 660 to 2,900 euros per pack at the beginning of the project, prior to the start of the orphan drug registration application, in order to finance its costs which are basically the estimated registration costs for the years 2014, 2015, and 2016. In fact, Sigma Tau did so in July 2014. The estimated cash flows take into consideration the planned increase in price to €5,000 once the designation of the drug was hypothetically done. Finally, from this, it is clear that Sigma Tau decided to go ahead with the application for orphan designation and AIC to market the orphan drug in Europe because the project's profitability was so high even with a sales price for the drug of no more than €5,000 per pack. As a result, it follows that increasing the sales price, as was really done, could only have widened the gap between prices and costs further.

From the above methodology applied by Sigma Tau for all Europe, the AGCM did an analysis of the excessiveness of the CDCA Leadiant® in Italy using the same methodology of the undertaking. Particularly, the IRR of the project was calculated based on the cash flows derived from the project, taking into account the ex-factory price applied by Leadiant to sales of Xenbilox® in Italy, equal to 2,900 euros, during the period between January 2016 and May 2017 as well as the ex-factory price of CDCA Leadiant®, equal to 15,506.93 euros, in the years from 2017 to 2019, during the drug's classification in class Cnn and starting from 2020, following the agreement with AIFA equal to in between 5,000 and 7,000 euros. In Figure 12 the revenues related to sales of Xenbilox® and CDCA Leadiant® in Italy are shown, using the actual and projected sales figures for Xenbilox® and CDCA Leadiant® provided by the Party for the years from 2014 to 2023 and assuming, favorably for the Party, that CDCA Leadiant® sales for the years between 2024 and 2027 would not increase from those of 2023.

Figure 12 CDCA project revenues in Italy (en.agcm.it)

Anno	Quantità Xenbilox® (Q^X)	Prezzo Xenbilox® (P^X)	Quantità CDCA Leadiant® (Q^{CDCA})	Prezzo CDCA Leadiant® (P^{CDCA})	Ricavi progetto CDCA Italia* (R^P Italia=Q^X* P^X + Q^{CDCA}* P^{CDCA})
2016	*[100-200]*	*2.900*			*[300.000-400.000]*
2017	*[50-100]*	*2.900*	*[100-200]*	*15.506,93*	*[2-3 mln]*
2018			*[300-400]*	*15.506,93*	*[5-6 mln]*
2019			*[300-400]*	*15.506,93*	*[5-6 mln]*
2020			*[300-400]*	*[5.000-7.000]*	*[2-3 mln]*
2021			*[300-400]*	*[5.000-7.000]*	*[2-3 mln]*
2022			*[400-500]*	*[5.000-7.000]*	*[2-3 mln]*
2023			*[400-500]*	*[5.000-7.000]*	*[2-3 mln]*
2024			*[400-500]*	*[5.000-7.000]*	*[2-3 mln]*
2025			*[400-500]*	*[5.000-7.000]*	*[2-3 mln]*
2026			*[400-500]*	*[5.000-7.000]*	*[2-3 mln]*
2027			*[100-200]*	*[5.000-7.000]*	*[800.000-900.000]*

For what concerns the costs of the project in Italy, the undertaking provided the costs aggregated at the European level, so the Italian ones were obtained on the basis of the share of sales occurring in Italy in relation to total sales, as shown in Figure 13.

Figure 13 CDCA project costs in Italy (en.agcm.it)

Anno	Costi Xenbilox® (C^X)	Costi CDCA Leadiant® (C^{CDCA})	Costi progetto CDCA (C^P=C^X+C^{CDCA})	Volumi Italia su volumi totali (%)	Costi progetto CDCA Italia (C^P Italia = C^P*% volumi Italia)
2014	*[200.000-300.000]*	*[1-2 mln]*	*[2-3 mln]*	*[10-15]*	*[200.000-300.000]*
2015	*[300.000-400.000]*	*[6-7 mln]*	*[7-8 mln]*	*[10-15]*	*[800.000-900.000]*
2016	*[50.000-100.000]*	*[7-8 mln]*	*[7-8 mln]*	*[10-15]*	*[900.000-1 mln]*
2017	*[1-50.000]*	*[7-8 mln]*	*[7-8 mln]*	*[10-15]*	*[900.000-1 mln]*
2018		*[7-8 mln]*	*[7-8 mln]*	*[10-15]*	*[900.000-1 mln]*
2019		*[10-20 mln]*	*[10-20 mln]*	*[10-15]*	*[1-2 mln]*
2020		*[10-20 mln]*	*[10-20 mln]*	*[5-10]*	*[1-2 mln]*
2021		*[9-10 mln]*	*[9-10 mln]*	*[10-15]*	*[1-2 mln]*
2022		*[7-8 mln]*	*[7-8 mln]*	*[10-15]*	*[900.000-1 mln]*
2023		*[6-7 mln]*	*[6-7 mln]*	*[10-15]*	*[800.000-900.000]*
2024		*[6-7 mln]*	*[6-7 mln]*	*[10-15]*	*[800.000-900.000]*
2025		*[6-7 mln]*	*[6-7 mln]*	*[10-15]*	*[800.000-900.000]*
2026		*[6-7 mln]*	*[6-7 mln]*	*[10-15]*	*[800.000-900.000]*
2027		*[1-2 mln]*	*[1-2 mln]*	*[10-15]*	*[200.000 - 300.000]*

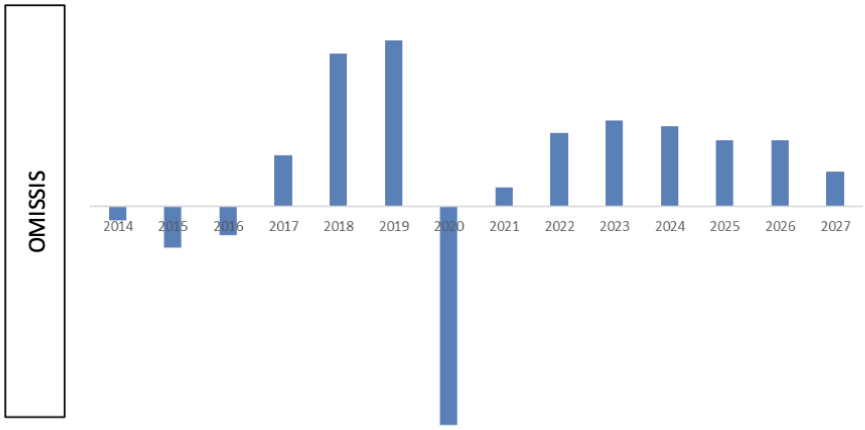
Finally, the IRR was calculated both by considering all cash flows derived from the realized revenue less the costs incurred for the project and only the incremental flows compared to those that would have been obtained with the continuation of off-label sales of Xenbilox®. The cash flows are determined from the difference between the revenues and costs, previously shown, both the ones effectively charged by the undertaking in between 2014 and 2020 and the expected ones from 2020 until the end of the exclusivity in, 2027. In Figure 14, the annual profits for Italy related to the CDCA project were calculated for this purpose, as the difference between project revenues and costs; the reimbursements to the SSN made by the Party in the execution of the agreement with AIFA and related to the difference between the price paid and the negotiated price were deducted from the profits for the years 2020 and 2021. Furthermore, the average tax rate paid by Sigma Tau between 2014 and 2019, as shown in the financial statements submitted by Leadiant Biosciences Ltd. and its principals was also applied to the profits, wich amounted to 21%. It should be noted that the rate employed here is the highest and, consequently, more advantageous to the Party compared to both that employed by Sigma Tau itself in the ex ante analysis, equal to 20%and of the average tax rate recorded in Europe in the pharmaceutical sector during the same period, equal to 19%. In addition, the change in net working capital (NWC) from the prior period was also deducted for each year. The approaches used to calculate the change in NWC were the ones adopted by Sigma Tau in its ex ante valuation model.

Figure 14 Cash flows of the CDCA Leadiant® project for Italy (en.agcm.it)

Anno	Utile progetto CDCA Italia (U^P Italia=R^P Italia – C^P Italia)	Utile progetto CDCA Italia al netto delle tasse	Variazione CCN	Flusso di cassa progetto CDCA Italia
2014	*-[200.000-300.000]*	*-[200.000-300.000]*	*0*	*-[200.000-300.000]*
2015	*-[800.000-900.000]*	*-[800.000-900.000]*	*-[1-50.000]*	*-[800.000-900.000]*
2016	*-[500.000-600.000]*	*-[500.000-600.000]*	*[1-50.000]*	*-[500.000-600.000]*
2017	*[1-2 mln]*	*[1-2 mln]*	*[300.000-400.000]*	*[1-2 mln]*
2018	*[4-5 mln]*	*[3-4 mln]*	*[500.000-600.000]*	*[3-4 mln]*
2019	*[4-5 mln]*	*[3-4 mln]*	*[1-50.000]*	*[3-4 mln]*
2020	*-[5-6 mln]**	*-[5-6 mln]*	*-[1-2 mln]*	*-[4-5 mln]*
2021	*[900.000-1 mln]***	*[900.000-1 mln]*	*[500.000-600.000]*	*[300.000-400.000]*
2022	*[1-2 mln]*	*[1-2 mln]*	*[50.000-100.000]*	*[1-2 mln]*
2023	*[1-2 mln]*	*[1-2 mln]*	*[1-50.000]*	*[1-2 mln]*
2024	*[1-2 mln]*	*[1-2 mln]*	*[1-50.000]*	*[1-2 mln]*
2025	*[1-2 mln]*	*[1-2 mln]*	*[1-50.000]*	*[1-2 mln]*
2026	*[1-2 mln]*	*[1-2 mln]*	*[1-50.000]*	*[1-2 mln]*
2027	*[600.000-700.000]*	*[400.000-500.000]*	*-[200.000-300.000]*	*[700.000-800.000]*

The trend of project cash flows that were reported to Italy between 2014 and 2027 is shown in Figure 15. The negative flows for the years 2014 to 2016 are due to the costs of preparing CDCA to receive orphan drug status and registering CDCA Leadiant® as an orphan drug to treat CTX. Sales of Xenbilox® at the higher price in Italy only partially offset these costs. The project has started to produce generally positive cash flows since 2017, with the exception of 2020, when the undertaking almost entirely repaid the sum agreed upon in the agreement with AIFA.

Figure 15 Cash flows of the CDCA Leadiant® project for Italy (en.agcm.it)



The internal rate of return for the project as a whole, from 2014 to 2027, has been determined to be between 50% and 60%. To ascertain if the project will be profitable, this value must be contrasted with the cost of capital (the WACC). In this situation, it was deemed permissible to apply the WACC number that Sigma Tau itself employed in its ex-ante study. Again, from the Party's standpoint, the highest value—the one linked with the "best case scenario"—which includes a higher risk element—equal to 15%—was taken into account. Considering that the average WACC seen for pharmaceutical businesses in Western Europe in 2014 was 10%, this value was regarded extremely concessive. Indeed, the sale price of CDCA Leadiant® in Italy produced a project rate of return of three to four times the cost of capital, according to the aforementioned study. The IRR analysis was also conducted using solely incremental cash flows as a reference, which are those attributable to the project and that, in the absence of the project, would not have occurred. This was done as an additional precaution for the Party. Only incremental revenues and costs, so the difference between revenues and costs attributable to the new product and revenues and costs related to the replaced product, that would have been incurred in the absence of the project, were taken into account in the current case since the project under assessment consists of the launch of a new product that replaces an existing product. In addition, other documents came to light that demonstrated that Sigma Tau would have continued to sell Xenbilox® administered off-label for the treatment of CTX if the orphan drug registration had

failed and that, in the absence of the project, no price increases for Xenbilox® were planned for the upcoming years. According to these documents, the revenues from the sale of Xenbilox® accounted for 2 million euros, and the ones from CDCA Leadiant® for 31 million euros. Therefore, the additional cash flows due to the CDCA project that had to be taken into account were those that differ from the case without the project itself, with the ongoing selling of Xenbilox® off-label at the then-current price of 660 euros per pack. Therefore, the revenues that would have been generated by selling Xenbilox® at 660 euros were subtracted from the revenues that the Party actually received or anticipated. Regarding the incremental expenses, which are the costs that would not have been incurred had the CDCA project not been undertaken, but Xenbilox® administered off-label sales continued, the Party supplied an estimate that did not seem reasonable for the CDCA initiative but that was used anyway; in fact, the total costs of CDCA Leadiant® were considered instead of the incremental ones, as provided by the undertaking. This choice was extremely favorable to the Party since incremental costs are by definition a subset of total costs. Figure 16 displays the incremental profits associated with the CDCA project, which are calculated by subtracting incremental revenues from incremental costs, as above motioned, in this case, are assumed to coincide with total costs. For the purpose of calculating incremental cash flows, CNN's after-tax profit and change were calculated in accordance with the procedures used to calculate total cash flows.

Figure 16 Incremental cash flows of the CDCA Leadiant® project for Italy (en.agcm.it)

Anno	Utile incrementale progetto CDCA Italia (R^P incrementali Italia – C^P incrementali Italia)	Utile incrementale progetto CDCA Italia al netto delle tasse	Variazione CCN	Flusso di cassa incrementale progetto CDCA Italia
2014	*-[200.000-300.000]*	*-[200.000-300.000]*	*0*	*-[200.000-300.000]*
2015	*-[800.000-900.000]*	*-[800.000-900.000]*	*-[1-50.000]*	*-[800.000-900.000]*
2016	*-[600.000-700.000]*	*-[600.000-700.000]*	*[1-50.000]*	*-[600.000-700.000]*
2017	*[1-2 mln]*	*[1-2 mln]*	*[300.000-400.000]*	*[800.000-900.000]*
2018	*[4-5 mln]*	*[3-4 mln]*	*[500.000-600.000]*	*[2-3 mln]*
2019	*[4-5 mln]*	*[3-4 mln]*	*[1-50.000]*	*[3-4 mln]*
2020	*-[5-6 mln]**	*-[5-6 mln]*	*-[1-2 mln]*	*-[4-5 mln]*
2021	*[600.000-700.000]***	*[600.000-700.000]*	*[500.000-600.000]*	*[100.000-200.000]*
2022	*[1-2 mln]*	*[1-2 mln]*	*[50.000-100.000]*	*[1-2 mln]*
2023	*[1-2 mln]*	*[1-2 mln]*	*[1-50.000]*	*[1-2 mln]*
2024	*[1-2 mln]*	*[1-2 mln]*	*[1-50.000]*	*[1-2 mln]*
2025	*[1-2 mln]*	*[1-2 mln]*	*[1-50.000]*	*[1-2 mln]*
2026	*[1-2 mln]*	*[1-2 mln]*	*[1-50.000]*	*[1-2 mln]*
2027	*[300.000-400.000]*	*[200.000-300.000]*	*-[200.000-300.000]*	*[400.000-500.000]*

Figure 17 shows the incremental cash flows of the CDCA project, obtained as described above, which are compared to the overall cash flows (Figure 14). The incremental flows are smaller than the non-incremental flows, because sales of Xenbilox®, which would have taken place anyway in the absence of the project, were not subtracted from the latter. The use of incremental cash flows is, therefore, favorable to the Party.

Figure 17 Incremental and total cash flows of the CDCA project for Italy (en.agcm.it)

The value of the IRR is equal to [40-50%] for the period from 2014 to 2027, the duration of the all project. The comparison between the project's IRR and the WACC confirmed not only that the project is remunerative for the dominant company but also that the first value is significantly higher than the second. Based on the analysis conducted, the internal rate of return IRR is at least [250-350%] of the cost of capital. The prices charged by Leadiant generate a project profitability three times the capital cost. This means that even considering all the favorable assumptions for the defendant, the sales of CDCA Leadiant® generated extremely high and excessive returns for the dominant company.

Accounting methodology

The second methodology used in the excessiveness analysis is based on a comparison between the sales revenues realized in Italy utilizing the price whose excessiveness is being assessed, in this case, the negotiated price between 5,000 and 7,000 euros, and the so-called cost plus, which corresponds to the costs, direct and indirect, incurred by the dominant company for Italy in relation to CDCA Leadiant® and includes a reasonable margin of profitability for the dominant company. The difference between the revenues and the cost-plus represents the excess (EXC) of which the disproportion had to be valued. The excess is then compared to the cost plus to obtain the percentage

value (EXC%) in order for it to be analyzed against other results in cases of excessive pricing. The metric of profitability was somewhat quantified for the case as a rate of return on sales of 21%, which was an extremely high benchmark, given the sort of project under investigation, which was characterized by lower levels of risk and investment with respect to the average pharmaceutical projects and it was, indeed, significantly higher than the ones utilized by the Authority in other cases. Furthermore, the price was set in between 5,000 and 7,000 euros, because the sales made to hospitals in the Cnn class were reimbursed for the difference between the price paid and the price negotiated with AIFA. Finally, as it can be seen from Figure 18, the percentage excess of revenues from sales of CDCA Leadiant® at the price of [5,000-7,000] euros over the cost plus was found to be [60-70%] for the period from the start of the commercialization of CDCA Leadiant® in Italy until the end of 2020 and [90-100%] considering as the end of the period the expiration of the market exclusivity, set in April 2027.

Figure 18 Calculation of the cost plus and excessiveness in percentage (en.agcm.it)

Anno	**Quantità CDCA Leadiant® (Q^{CDCA})**	**Prezzo CDCA Leadiant® (P^{CDCA})**	**Ricavi CDCA Leadiant® (R^{CDCA}= P^{CDCA}*Q^{CDCA})**	**Costi CDCA Leadiant® (C^{CDCA})**	**C^{+} (C^{CDCA}/(1-ROS))**	**EXC % ((R^{CDCA} – C^{+})/C^{+})**
2026	*[400-500]*	*[5.000-7.000]*	*[2-3 mln]*	*[800.000-900.000]*	*[1-2 mln]*	*[100-150%]*
2027	*[100-200]*	*[5.000-7.000]*	*[800.000-900.000]*	*[200.000-300.000]*	*[300.000-400.000]*	*[150-200%]*
giu 2017-dic 2020	*[1.000-2.000]*	*[5.000-7.000]*	*[7-8 mln]*	*[3-4 mln]*	*[4-5 mln]*	***[60-70%]***
giu 2017-apr 2027	*[3.000-4.000]*	*[5.000-7.000]*	*[20-30 mln]*	*[10-20 mln]*	*[10-20 mln]*	***[90-100%]***

In conclusion, both approaches utilized in this study lead to a similar conclusion regarding the significant discrepancy between the prices levied by the dominant company and the associated costs incurred. Additionally, this disparity is notably greater than the thresholds identified as abusive in the previous rulings that established violations of Article 102(a) of the Treaty on the Functioning of the European Union

B. Unfair prices

This section aims to investigate whether non-cost related factors exist that could justify the significant discrepancy in prices. If such factors are deemed invalid, the prices charged by Leadiant would lack a reasonable relationship with the economic value of the service provided and would be deemed unfair. For the reasons that will be explained below, it is deemed more appropriate, in this particular case, to opt for an evaluation of the unfairness inherent in Leadiant's pricing policy, rather than a

comparative evaluation. In fact, the European Commission abstractly considered the possibility of applying the formulation adopted by the Court, which considered “competing products”, through two second-best options: comparing the price of the same product sold by the same company in other markets or comparing the price of "similar products" sold in other markets, in cases where no "competing products" can be identified, for example, products belonging to the same relevant market as the product under examination. For Leadiant® CDCA in this case it is not possible to consider "competing products" in a potential price comparison activity. Therefore, in order to value the practice of the European Commission and the case law of the Court of Justice and look at the price of orphan drugs indicated as comparable to Leadiant® CDCA by the Party, the following has been observed:

a. Comparison with similar products:

Firstly, it is important to consider that both the European Commission and the Court of Justice have established that, in order to avoid inappropriate comparisons, similarities between products must be evaluated under homogeneous conditions. In other words, the products considered similar must be truly comparable, so that the comparison is valid and the results are significant. Therefore, the conditions under which the comparison is made are of fundamental importance. In fact, the comparative analyses conducted have to take into account the number of patients taking the drugs included in the two groups considered. In other words, the prices of these products are determined by unknown epidemiological data that are presumed to be distinct. However, it is known that the definition of the price level of a given drug is necessarily influenced by the size of the demand, since volumes, together with price, determine the overall impact on the National Health System's budget, as evidenced by the facts that characterized the negotiation of the price of Leadiant® CDCA. Finally, it is necessary to adequately consider the innovative nature of some orphan drugs included in the larger sample. The distinction between drugs that, like the orphan drug in question, are so-called repurposed, and drugs based on newly developed unknown active ingredients, is not irrelevant. The two categories of drugs differ, in fact, in the amount of resources invested in their development. As recognized by the European Commission, investment in research and development for repurposed orphan drugs is much lower than that for completely new orphan drugs. This explains why they should marketed on average at lower prices, as can be seen from the data produced by Leadiant itself in its statements. Failing to separately consider the category of innovative drugs from non-innovative drugs leads, therefore, to taking, as the Party does, an overestimated and therefore unsuitable point of comparison for the assessment of the unfairness of the price of Leadiant® CDCA. It should also be noted that the unsuitability, for the purpose of evaluating the unfairness of Leadiant's pricing policy, of the comparative analysis proposed by the Party also arises from certain documents in the case file.

For example, research commissioned by the dominant firm in October 2015 showed that the stakeholders interviewed (health economists, doctors, and pharmacist consultants for national regulatory authorities) were extremely reluctant, if not even "offended," by Sigma Tau's consultants' attempt to compare the price of the future orphan drug with drugs registered for other ultra-rare. It should also be noted that among the drugs proposed as a comparator, and rejected by the stakeholders, was Orphacol.

b. The comparison with Orphacol:

Regarding the comparison proposed by the opposing party between the Orphacol drug and the CDCA Leadiant®, it is important to emphasize that this does not represent a correct application of the judgment of the EU Court of Justice, cited by Leadiant. In that decision, the Court hypothetically considered the possibility of comparing two identical services provided in two different markets, where the difference was that one was under concession and the other was in competition. Therefore, the Court hypothesized that the unfairness of the price at which the concession service was provided could be evaluated by comparison with a competitive benchmark. However, in this case, the opposing party proposes a comparison between products that both have a market exclusivity, the orphan drug designation, which by definition allows them to benefit from a significant mark-up. In other words, Orphacol cannot be considered a competitive benchmark providing adequate indications about the unfairness of the price of CDCA Leadiant®. Apart from this crucial observation, it is evident that the opposing party's conclusion that Orphacol is more expensive than CDCA Leadiant® by [50-60%] is based on erroneous or unverified assumptions. The conclusion about the comparability of the two drugs is firstly based on the assumption that since Orphacol is a repurposed drug, the registration costs are similar or even lower, given that it is a procedure based on the so-called well-established use, mainly based on scientific literature. However, this remains an unproven assumption not substantiated by Leadiant in any way. Furthermore, a careful analysis of public sources should have led the opposing party to realize that the data of 2,300 patients that they claimed used Orphacol refers to all congenital errors in the synthesis of primary bile acids, of which the two congenital defects treated with Orphacol represent only a small part. The specific prevalence of the two congenital defects that Orphacol intends to treat is, in fact, 3-5 patients per 10 million, for one defect and 0.3-0.5 patients per 10 million for the other defect. Applying the percentage of prevalence of rare diseases to the Italian population, the patients affected in the domestic market by the two congenital defects mentioned above would be about 12-20 patients, while the patients affected by CTX, according to what Leadiant itself claims, are [40-50], a number more than double, if not triple, which easily explains the price differential of about [50-60%] existing between the two drugs.

c. Comparison between the price of CDCA Leadiant® in the other member states

It is not deemed appropriate to evaluate the fairness of the price of CDCA Leadiant® in Italy by comparing it to the prices of the same drug in other European countries such as UK, France, and Germany, identified by the Party. The investigation conducted clearly indicates that Sigma Tau/Leadiant has implemented a pan-European commercial strategy, which is subject to scrutiny under antitrust laws by several national competition authorities. The foreign prices of CDCA Leadiant® may therefore be the result of the dominant company's strategy as much as the price practiced in Italy. Comparisons across borders in the pharmaceutical market, in general, risk not meeting the homogeneity criterion required by EU case law because they occur in a context of strong economic, institutional, and epidemiological heterogeneity that still characterizes the national pharmaceutical markets of the European Union. The European pharmaceutical market is characterized by persistent price differentials from one Member State to another, linked not only to the pricing differentiation strategies implemented by pharmaceutical companies, which should reflect the price elasticity of demand, based on willingness to pay and market size, but also, and above all, to the institutional and economic differences that inform different national pharmaceutical policies. In this context, it is evident that comparing the prices of the same product in various EU Member States does not provide any significant or indicative results of the fairness or unfairness of the price of that product in any of these Member States. Such structural differences, also related to the number of patients, emerge from the same evaluations of the dominant company and are also observed in relation to the prices currently applied for the orphan drug. For example, the price of CDCA Leadiant® in the UK was negotiated by Leadiant with the NHS in front of a number of CTX patients of about 24, almost half of Italian patients. This, together with a very different willingness to pay of the British NHS, explains why the price of CDCA Leadiant® in the UK is almost double compared to the Italian price (equal to [10,000-20,000] pounds per 100 capsules of 250 mg). In light of all these considerations, it is believed that, in this case, the homogeneity circumstances required by the practice of the European Commission and the case law of the Court of Justice of the European Union do not occur to make a comparative assessment of the unfairness of the price practiced by Leadiant for the orphan drug.

d. Unfairness of the price of the CDCA Leadiant®

Based on the above, it is believed that there is ample evidence in the proceedings to assert that the prices practiced by the dominant company for CDCA Leadiant® in Italy are inherently unfair. These are qualitative factors related to the nature of the product, the investments in research and

development made by the Party, the added therapeutic value of the orphan drug compared to pre-existing therapies - not measurable through the consumer's willingness to pay, since the willingness to pay for life-saving drugs without therapeutic alternatives tends towards infinity, making any price level plausible - and the effects of the conduct on the National Health Service (SSN).

Firstly, CDCA Leadiant® is a repurposed drug, meaning that its molecule already existed on the market for a certain therapeutic indication and was reintroduced with a new therapeutic indication. Therefore, it cannot be considered as a completely new medicinal product on the market. This is to acknowledge that even though CDCA Leadiant® has a specific registration for the treatment of CTX and an orphan designation compared to previous therapeutic alternatives, it cannot be regarded as a completely new drug. It is worth noting that even after the modifications to the production process, CDCA Leadiant® remains equivalent to Xenbilox®, and even to the magistral preparations of the Pharmacy of the AOU Senese, in terms of chemical and pharmaceutical properties. The three drugs have the same active ingredient, the same dosage, are produced based on the same raw material and by the same chemical company, and are bioequivalent. This is evident from the documents collected in the proceedings, which indicate that although there are some differences in excipients between the capsules produced by the Pharmacy and Xenbilox®, the two drugs are essentially similar, as recognized by the EMA based on the comparability studies carried out by the same dominant company. Furthermore, other documents collected during the investigation indicate that there is a relationship of equivalence, or even identity, between Xenbilox® and CDCA Leadiant®.

Another factor to highlight is that the Party did not incur significant research and development costs that could justify the initial price requested from AIFA or the one later negotiated with the Agency. Although the two retrospective studies conducted by AOU Senese and the Dutch hospital Casinius Wilhelmina of Nijmegen are essential for the understanding of the rare disease, it should be noted that they were carried out by public institutions with extensive clinical experience in administering CDCA to affected patients over more than forty years. The financial effort made by Leadiant to compensate for this activity and experience was quite minimal, with figures amounting to 300,000-400,000 euros and at most, in the future, 500,000-600,000 euros. Additionally, the activities carried out by PCA on behalf of Sigma Tau to implement the purity test developed by the dominant company for the improvement of CDCA production required minimal expenditure. The dominant company declared that it paid PCA an amount of 300,000-400,000 euros. These investments are extremely limited and, although they can benefit patients, they do not represent a "significant innovation". The

production process of CDCA as an active pharmaceutical ingredient remains relatively simple, and these investments cannot justify the price requested from AIFA for the orphan drug.
In addition, several documents demonstrate that the investments in R&D planned by Leadiant over time as the CDCA project progressed have always been very limited. These investments are not only modest in absolute terms but also when compared to most investments related to other drugs in the dominant company's portfolio and the total research and development investments they planned to support. The Copenhagen Economics study also revealed that the costs classified as research and development within the CDCA project are less than 1% of the total cost supported by the dominant company. For what concerns the direct costs associated with the production of the orphan drug, they are not significant, despite the increased compensation due to PCA for the purchase of raw materials. Furthermore, the costs related to scientific information activities are almost negligible, and it is not believed that the pharmacovigilance activity of the orphan drug is particularly expensive since it is a function that the dominant company already performed for its other products. Regarding the direct costs related to regulatory activities, which account for 30-40% of the total, it is observed that they mostly derive from activities that have composed Leadiant's strategy for pursuing its pricing policy. This means that a large part of the costs on which the dominant company believes it can justify the prices in Italy for the orphan drug are related to activities that represent the abuse contested to Leadiant.

Lastly, it is considered that the costs and risks that Leadiant claims to have faced within the CDCA project were not taken into account by the EMA for the granting of orphan designation. There is no evidence that the prices requested by the dominant company are necessary to compensate for the investments made and the risks faced, and that lower prices would reduce the incentive for innovation and the value of the orphan designation granted by the EMA. On the contrary, the documentation shows that even with a lower price than the one actually applied, the incentive to undertake the investment was significant. Leadiant estimated a particularly high NPV even with a price of 5,000 euros per package. This means that Leadiant would have had the incentive to undertake the project even with a substantially lower price, which would have allowed covering the costs and ensuring a profit margin for the dominant company while compensating for the risks faced. In other words, the excessive price set by Leadiant cannot be justified by the need to stimulate the incentive to undertake the registration project, as even at a price of 5,000 euros, the project was already highly profitable, and the risk was already widely compensated. In addition, these investments did not lead to achieve added therapeutic value compared to pre-existing therapies on the Italian market like the Xenbilox® and the magistral preparations produced by the Pharmacy of the AOU Senese. This clearly emerges

from several elements. Among the three recalled drugs, there is, in fact, a relationship of identity from a therapeutic point of view. This was first incisively confirmed by the medical specialist in the hearing, who declared that in his clinical experience, based on the administration in the last forty years first of the magistral preparation produced by the Pharmacy of the AOU Senese, then of Xenbilox® and finally of CDCA Leadiant®, there is no difference of a therapeutic nature between them. Some documents on file prove, moreover, that the dominant company itself was aware that the orphan drug did not have added therapeutic value compared to Xenbilox®: in fact, Sigma Tau did not want to subject the orphan drug to the added therapeutic value assessment procedure carried out by the competent German authorities in relation to newly introduced drugs on the market. And when the dominant company explored the hypothesis of requesting the added therapeutic value assessment procedure, it was advised against it: according to consultants, the outcome of the added therapeutic value assessment procedure was uncertain, precisely given the lack of clinical studies to support it. Particularly indicative in this context appears the fact that the consultants suggested to the dominant company to request the activation of the assessment procedure only if it was convinced it could demonstrate significant added value that would justify the envisaged price increase that it intended to apply for the orphan drug. In essence, the added value resulting from Leadiant's activity, therefore, consists in having formalized the therapeutic indication with which the drug had already been administered for decades to patients with CTX. In other words, this activity allowed the transition from off-label to on-label treatment. Regarding the argument of the Party that believes it is necessary to give adequate recognition of the value that the CDCA Project has brought to patients and the NHS, precisely thanks to the registration of the rare therapeutic indication, the following is noted.

According to AIFA, the registration of the orphan drug achieved through the CDCA Project was in itself socially useful, but it is not sufficient, either in terms of the resources used or the actual result achieved, to justify the prices requested by the dominant company for the sale of the orphan drug in Italy. In addition to the fact that Leadiant's activity was significantly predominantly based on activities other than innovation, it should also be emphasized that the registration of the therapeutic indication, while undoubtedly bringing benefits to patients, cannot in any case lead to affirming, as the Party does, that Leadiant would have formally demonstrated for the first time the efficacy and safety of the drug and its risk and benefit profile. On the contrary, given that it, albeit for understandable reasons, did not carry out controlled prospective studies with placebo, the efficacy and safety profile and risk / benefit ratio of CDCA in the treatment of CTX is scientifically still not completely known. This is in fact what the expert consulted by the dominant company stated in his opinion, who declared that "In fact, comprehensive evidence [...] was not even established at the time the MA was granted". It

would not otherwise be explained why the European Commission granted the orphan drug's MA "under exceptional circumstances", whereas the majority of orphan drugs are authorized with a "full" AIC. The conditional release of the administrative title is in fact aimed precisely at monitoring over time the efficacy and safety of the drug, since at the time of attribution of the AIC this had not been demonstrated. This circumstance was expressed even more clearly by the Commission de la transparence of the Haute Autorité de Santé, which, in order to identify the added therapeutic value of CDCA Leadiant®, found that the efficacy data presented by the dominant company were very limited and weak, as they were based on the retrospective analysis of the medical records of some groups of patients treated with CDCA-based drugs with discordant results on clinical symptomatic criteria, and that data on clinical morbidity and mortality criteria as well as comparative data were lacking. So much so that, as already illustrated, the Commission determined that the orphan drug has low added therapeutic value and had not brought any improvement or had brought no significant improvement from a therapeutic point of view compared to the past, deserving a reimbursement price equal to 30% of the negotiated price. It is important to note that the French authorities' refunded price for the drug CDCA Leadiant® was of a similar magnitude to the price deemed acceptable by AIFA for the dominant company to sell the drug in the Italian market. It is also emphasized that the price levels identified by the two national regulators are higher than those identified based on the 2008 and 2014 assessments of the appropriate remuneration for the orphan drug. Market research conducted in 2008 indicated that the "reasonable" price for the orphan drug was 1,327 euros per package. Similarly, market research commissioned by Leadiant in 2014 suggested that the "reasonable" price for a CDCA-based drug registered for the treatment of CTX in Italy could be around 1,300-1,800 euros per package, in line with the 2008 evaluation. The introduction price of CDCA Leadiant® on the Italian market and the subsequently negotiated price with AIFA are significantly far from the drug's assessed value by demand. Leadiant was aware that the requested price exceeded what could be considered adequate economic compensation for its activity and its fears were realized when the drug was introduced to the domestic market at an ex-factory price of 15,506.93 euros per package. Treating physicians reacted negatively to the price, considering it "extremely burdensome" and "unacceptable." In conclusion, from the above considerations, the price charged by Lediant was unfair.

vi. Case conclusion

In conclusion, the inquiry has foremost enabled to determine that Leadiant had a dominant position, which was obtained since the start of 2016, in the Italian market for CDCA-based medications

intended to treat a rare condition, CTX. In addition, in light of the above, it was assessed that Leadiant violated Article 102(a) TFEU by imposing unfair prices for the sale of the orphan drug CDCA Leadiant® to the SSN by abusing its dominant position in the domestic market for the production and sale of CDCA-based drugs for the treatment of CTX. Leadiant's ultimate goal was, previously cited, to obtain the orphan designation of the CDCA-based drug that was previously used off-label for the treatment of CTX, was achieved thanks to a contractual agreement between Leadiant and the only credible provider of CDCA, PCA; this made it the only company that provided the drug in Europe. Furthermore, by labeling the orphan drug, it assured itself a monopoly until 2027, which strengthen its dominant position. The illegal activity occurred using a sophisticated and well-articulated commercial and regulatory strategy, which also included acting obstructively and dilatorily toward AIFA during discussions about the orphan drug's price. This abuse immediately cost the SSN money because it resulted in the procurement of a life-saving medicine at an exorbitant price. Leadiant argued in defense of its position that the drug's budget was absolutely insignificant and that, during the negotiation process, it made an agreement with AIFA and the ASLs to return any difference between the price charged while waiting for an agreement to be reached and the price that would then be negotiated with the Agency. There is no mention of Leadiant's unwillingness to harm the SSN, since the amount of the price differential to be returned depends on the level of the negotiated price, but it is noted that this commitment is typical in negotiations between pharmaceutical companies and AIFA. On the other hand, it should be highlighted that despite the orphan drug's modest budget, Leadiant's significant excess in relation to its economic value had a direct impact on the SSN's meager funds set aside for pharmaceutical spending. Therefore, the AGCM fined Lediant 3,5 million euros, for its abuse of its dominant position by charging an excessive and unfair price for the lifesaving drug, CDCA Leadiant®.

5. Conclusions

Over the past few years, Antitrust Authorities have increasingly been handling instances of excessive pricing in the pharmaceutical sector. Thanks to their interventions they safeguard consumers' interests which are not always protected by pharmaceutical companies, despite the importance and uniqueness of their products, which are essential for patients' health and well-being, in particular when there are no alternative treatments available. In fact, the role of Antitrust Authorities in cases of excessive pricing in the pharmaceutical industry is crucial in ensuring that patients have access to affordable and effective treatments. By promoting competition and preventing monopolies, antitrust authorities help to ensure that pharmaceutical companies are incentivized to develop new and innovative treatments while also keeping prices reasonable and accessible to patients, whenever regulation may not be effective against dominant abuses. At the same, it is also important to add that it is extremely difficult for authorities to address excessive pricing abuses in a complex sector like the pharmaceutical one. Indeed, it is extremely complicated to determine metrics that enable the Authorities to assess whether a price is excessive and unfair, as they vary from case to case and there is no rule of thumb applicable. In addition, so far, competition authorities have primarily directed inquiries into exorbitant pricing toward older, off-patent drugs which don't incur significant R&D costs. However, with the rise of personalized medicine and a growing focus by pharmaceutical companies on orphan treatments, competition authorities face mounting pressure to use competition economics to address this issue, which is ultimately a regulatory matter.

With regards to the above, the first conclusion to address, concerns the question pointed out before: is implementing competition policy an appropriate approach for managing excessive pricing in the pharmaceutical industry? As we saw in the previous sections some people think that competition law should not interfere in the pricing field but trust the market's self-correcting capability. Conversely, some favor antitrust intervention as the best way to protect consumer welfare. From the analyses above, it can be evinced that the role of the Antitrust Authorities in dealing with cases of excessive pricing, especially in the pharmaceutical sector, is essential. First of all, due to the fact that the industry has different characteristics from the others, as they provide products that are crucial for people and, consequently, for which, their willingness to pay cannot be taken into consideration. In addition, medicines costs are, most of the time, a burden for government spending and not for the final consumer itself. On top of that, pharmaceutical companies must be provided which incentives to discover or innovate drugs, and for this reason, in particular, for orphan drugs, the undertakings are supplied with exclusive rights that guarantee them monopoly power. This precludes the industry from the self-correcting abilities previously discussed and puts authorities in a difficult position as

they have to deal with excessive pricing while at the same time being on guard to not distort the incentives to innovate. On the other hand, for generic drugs the economic theories of self-adjustment through competition should apply, but, as it can be seen from the Aspen instance, it is not always the case. Furthermore, the role of regulation, which provides ex-ante control in terms of excessiveness, is very limited. As we saw in both Aspen and Leadiant cases it is extremely likely that an undertaking in a dominant position will use strategies that exploit its power in order to negotiate with regulatory bodies. For all of the above reasons, the Authorities' interventions are probably the best way to address cases, ex-post, of abuse through excessive pricing that couldn't be managed by regulation. At the same time, the ex-ante, regulatory policies should be improved in order to make antitrust interventions necessary only in extreme cases.

For Authorities, the definition of price excessiveness and the determination of which analysis to use according to the case on hand, represent huge limitations. In the Leadiant and Aspen cases, for example, different methodologies had been used by the AGCM to assess pricing unfairness and excessiveness. In particular, for the latter, the analysis of excessiveness was conducted through an ex-post methodology by comparing the costs and prices incurred by the undertaking, through the contribution margin analysis. For Leadiant the IRR analysis was used to assess excessiveness. The IRR is typically done ex-ante, or before a project even starts, to help a corporation determine whether to proceed with it. Indeed, at the outset of the project, Sigma Tau itself carried out a financial study of the net present value of the CDCA project at the European level. By definition, the cash flows taken into account in an ex-ante analysis are based on the company's expectations for expenses and revenues. In the Leadiant case, the AGCM, thanks to inspections, used for the IRR analysis the discount rate that the company itself considered appropriate in the ex-ante analysis of project profitability. In particular, the AGCM addressed most of the analyses on statements made ex-ante by the company, such as the use of the WACC, for the calculation of excessiveness, determined from the undertaking before the start of the project and that, consequently, takes into consideration also the risk valuation done by the undertaking. The use of helpful metrics for Leadiant by the AGCM, using the ex-ante assumptions made by the undertaking and not the ex-post results of the company, in particular in terms of profitably, is mainly driven by the difference between the two companies under consideration. Indeed, the fact that different methodologies were applied in the two cases is mainly caused by the distinctions between Aspen and Leadiant. In fact, the former, was responsible for an abuse of dominance by charging excessive pricing in off-patent generic drugs, for which competition limitation was therefore not granted, for the latter a right to have protection from competition in the European market was granted for ten years. This is provided by law in order to compensate companies

investing in rare diseases and to encourage innovation in an area that has little commercial interest. In this case, it is important for Authorities to not distort the incentive to innovate, since the company has the right to be the only supplier of the drug for the established period and for the assessed therapeutic indication; the AGCM, as shown in detail by the official case summarized above, guaranteed a higher margin of profitability by making assumptions always favorable for the undertaking. In this way, Leadiant was granted by the Authority with a higher benchmark price in terms of excessiveness, in order to incentivize the undertaking to invest in innovation, being the only one able to sell the drug. In fact, the market under consideration is small as the drug is used to treat a rare disease, and the company must be encouraged to stay in the market and incentivized to innovate the product, for this reason the undertaking is provided with exclusivity. The Authorities took into consideration these factors before determining which methodologies, assumptions, and metrics to use to assess if the undertaking was abusing through excessive pricing of its dominant position.

To summarize, authorities are a viable option in addressing instances of abuse by dominant companies when regulatory measures have failed. However, relying solely on antitrust intervention is not the optimal solution. Instead, ex-ante price regulators should be improved at the national or European level to support regulatory measures and prevent price excessiveness. Antitrust authorities must only be used as a last resort in rare cases where regulations cannot prevent excessive pricing. While authorities possess significant power to handle excessive pricing, they must also be mindful of not undermining innovation incentives. The AGCM's decision in the Leadiant case to use ex-ante analyses of the company's pricing practices to determine excessiveness is an effective approach that safeguards innovation incentives, and that should be adopted similarly by other authorities. In addition, in the Leadiant case, the AGCM was able to get pieces of information on the WACC and other ex-ante measurements done by the undertaking in order to preserve incentives, but without this knowledge it would be extremely hard for authorities to do an equally robust analysis. The discount factor used in the IRR, for example, would have been really difficult to estimate by the AGCM, and consequently, it would have been really hard for the authority to do an appropriate analysis for the case. This is another reason why regulation should be the primary approach to address excessive pricing, and antitrust intervention should serve as a complementary measure.

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